Ospedale Luigi Sacco
POLO UNIVERSITARIO

Sistema Socio Sanitario
Regione Lombardia
ASST Fatebenefratelli Sacco

UNIVERSITAS STUDIORUM MEDIOLANENSIS

Switch a regimi TAF-based: dati dalla *real life*

Stefano Rusconi

Divisione Clinicizzata di Malattie Infettive

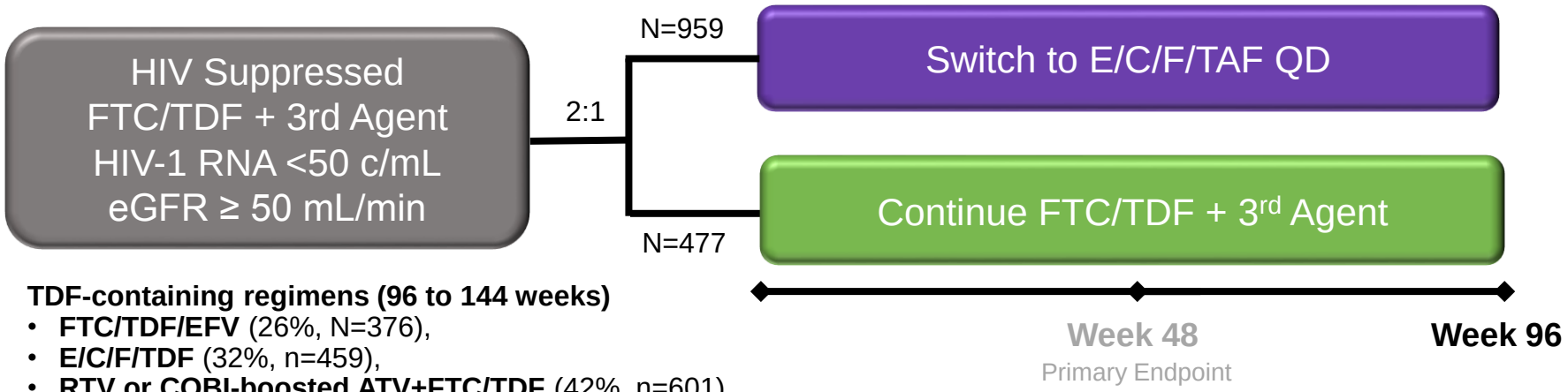
DIBIC Luigi Sacco

Università degli Studi di Milano

GIORNATE INFETTIVOLOGICHE «LUIGI SACCO» 2019, 28-29 MAGGIO

Study Design

Phase 3, 96-week, multi-centered, randomized, open label, active-controlled



TDF-containing regimens (96 to 144 weeks)
- **FTC/TDF/EFV** (26%, N=376),
- **E/C/F/TDF** (32%, n=459),
- **RTV or COBI-boosted ATV+FTC/TDF** (42%, n=601)

Primary Endpoint

Non-inferiority (12% margin) of switch to E/C/F/TAF vs continuation of baseline regimen by FDA Snapshot analysis (HIV-1 RNA <50 copies/mL at Week 48)

Secondary Endpoint

Efficacy and safety through Week 96[1]

Sub-analyses

Changes in bone biomarkers[2]

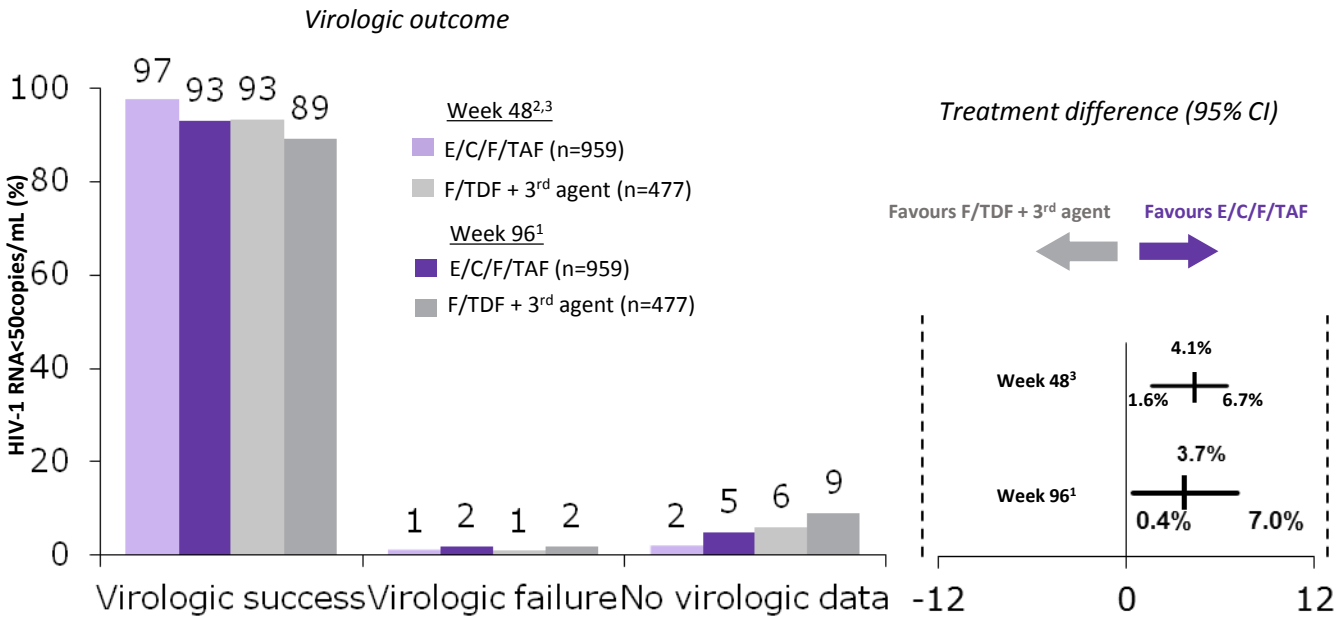
Safety and efficacy by D:A:D CKD risk categories[3]

1. DeJesus E, et al. ASM 2016. Boston MA. #087LB
2. Overton T, et al. ASM 2016 Boston MA. #411
3. Huhn G, et al. ASM 2016. Boston MA. Oral
4. Mills, A, et al. Lancet 2015.

ClinicalTrials.gov Identifier: NCT01815736

Study 109: ART-suppressed adults switched to E/C/F/TAF

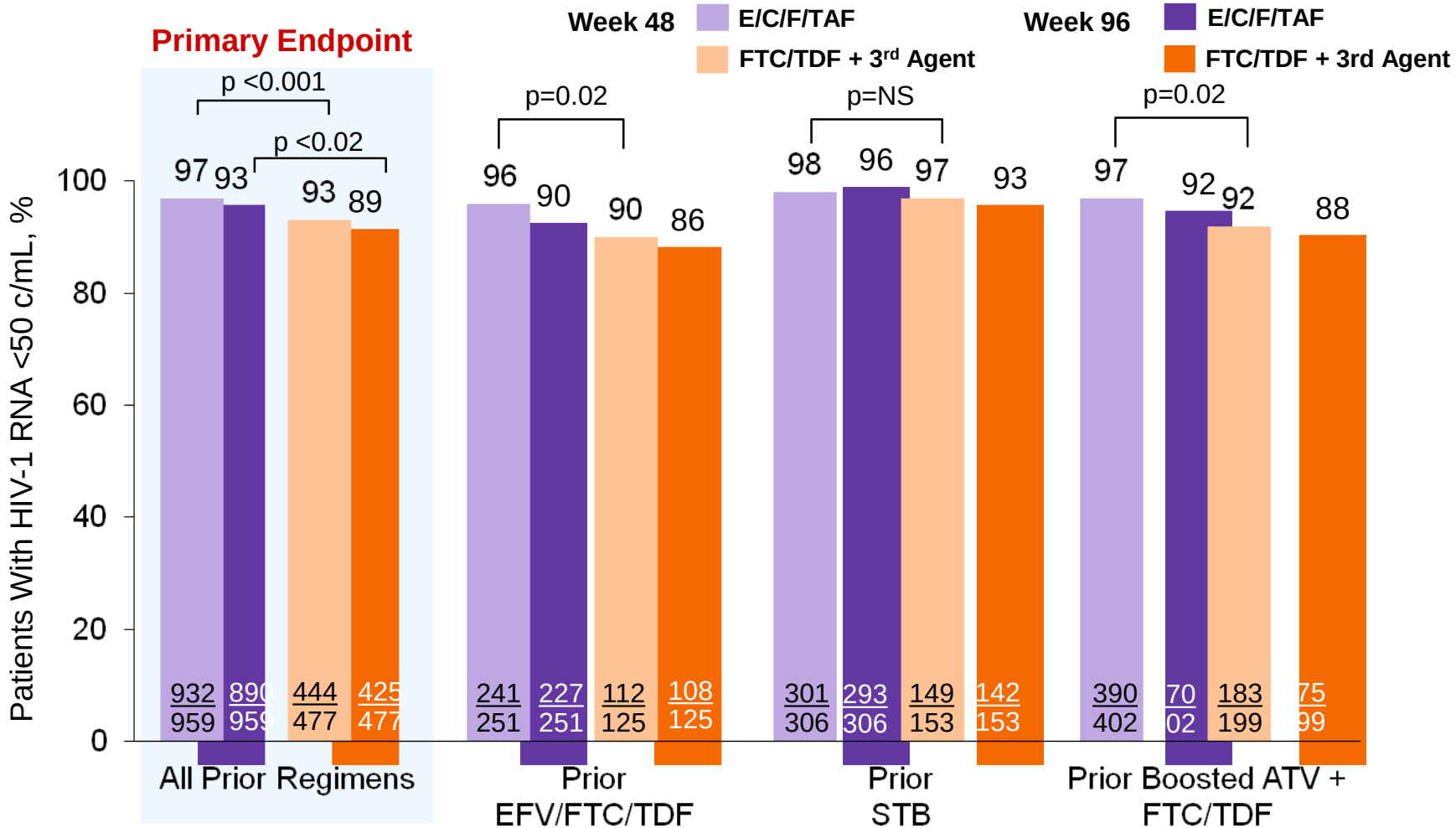
Virologic outcomes (HIV-1 RNA<50copies/mL) at Week 96



Patients who switched to E/C/F/TAF were significantly more likely to maintain virologic success compared to continuing F/TDF+3rd agent treatment through Week 96[1]

1. DeJesus E et al. ASM 2016. Boston MA. #087LB; 2. Mills A et al. Lancet Infect Dis 2016;16:43–52;
3. Mills A et al. IAS 2015. Vancouver, Canada. # TUAB0102

Virologic Outcome by Prior Treatment Regimens at Week 96

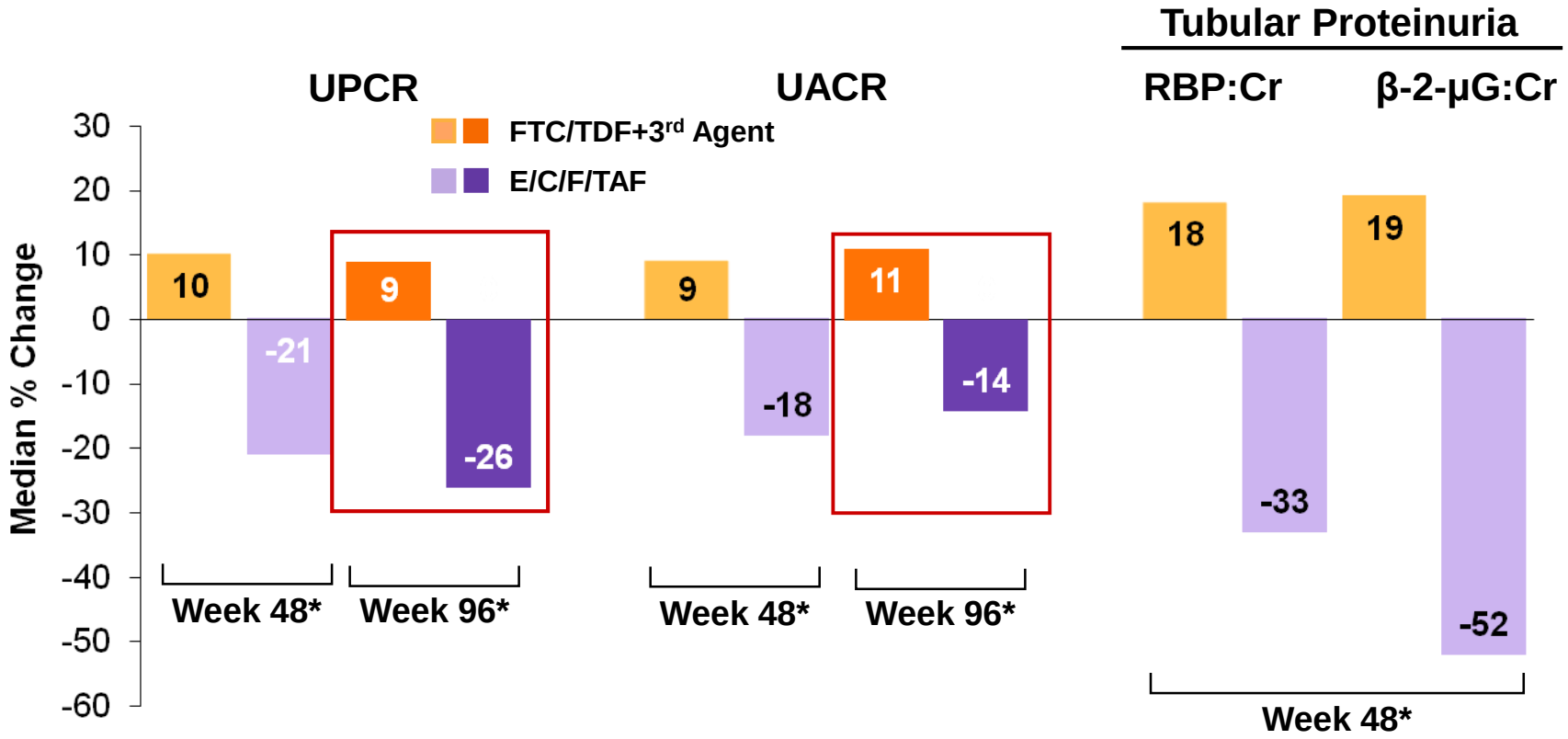


Week 48	95% CI =	1.6—6.7	0.5—12.3	-1.9—3.9	0.9—9.2
Week 96	95% CI =	0.4—7.0	-3.0—11.1	-1.7—7.6	-1.1—9.3

1. Mills A, et al. IAS 2015, Vancouver, Canada. Oral # TUAB0102
2. Shamblaw D, et al. ICAAC 2015, San Diego, CA. Oral
3. Thompson M, et al. ID Week 2015. San Diego, CA. Oral# 725
4. Rijnders B, et al. EACS 2015. Barcelona, Spain. Oral # PS10/3
5. DeJesus E, et al. ASM 2016. Boston MA. #087LB

‡

Changes in Quantitative Proteinuria Through Week 48 and 96



*Each difference between treatment arms was statistically significant (p <0.001)

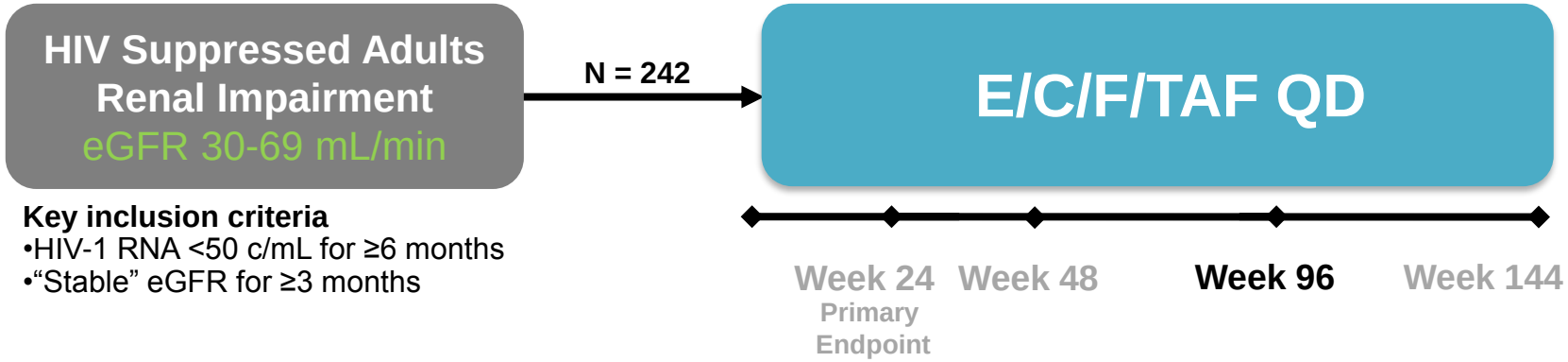
Switching to E/C/F/TAF from a regimen containing FTC/TDF+3rd agent resulted in significant decreases in proteinuria and albuminuria at Week 96

*RBP:Cr and β-2 μG:Cr were not measured at 96 weeks
UPCR= Urine Protein:Creatinine Ratio; UACR= Urine Albumin: Creatinine Ratio; RBP:Cr= Retinol Binding Protein: Creatinine Ratio;
β-2-μG= Cr: β-2-microglobulin:Creatinine Ratio

1. DeJesus E, et al. ASM 2016. Boston MA. #087LB
2. Mills A, et al. IAS 2015, Vancouver, Canada. Oral # TUAB0102

Study Design

Phase 3, 144-week, multicentered, single-arm, open label study



Key inclusion criteria
- HIV-1 RNA <50 c/mL for ≥6 months
- "Stable" eGFR for ≥3 months

Primary Endpoint

Change from baseline in glomerular filtration rate at Week 24

Secondary Endpoints

Efficacy, safety, and tolerability observed through Week 144

Sub-analyses

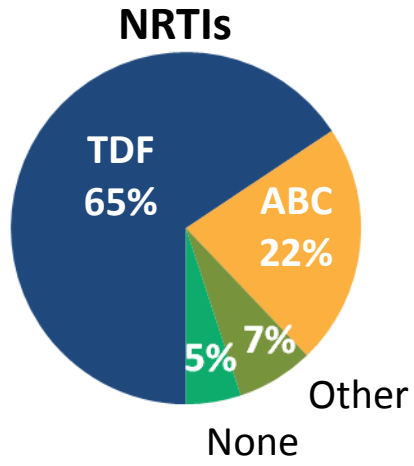
Safety of E/C/F/TAF in subjects who switched from a TDF or non-TDF-containing regimen[1]
Safety of E/C/F/TAF in subjects with baseline eGFR 30-49 mL/min compared to 50-69 mL/min[2]
Safety and efficacy of E/C/F/TAF in HIV suppressed women vs men with renal impairment[3]
Safety and efficacy of E/C/F/TAF in HIV suppressed diabetics with renal impairment[4]

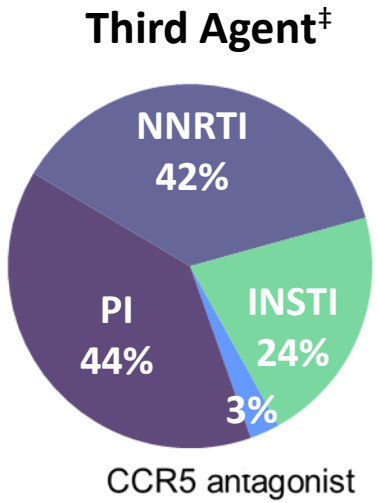
1. Post F, et al. CROI 2016. Boston MA. #680
2. Gupta S, et al. IAS 2015. Vancouver, Canada. Oral#TUAB0103
3. McDonald C, et al. ASM 2016. Boston MA. Oral
4. Stein D, et al. ASM 2016. Boston MA. Oral
5. Pozniak A, et al. JAIDS 2016.

ClinicalTrials.gov Identifier: NCT01818596.

Baseline Characteristics

Baseline eGFR category	<50 mL/min n=80	≥50 mL/min n=162
Median age, y (range)	59 (31–82)	58 (24–76)
Age ≥65 y, n (%)	25 (31)	38 (23)
Female, n (%)	21 (26)	29 (18)
Black or African descent, %	18	19
HIV-1 RNA <50 copies/mL, %	98	98
Median CD4 count, cells/µL	622	635
Pre-switch TDF, %	58	69
TDF dose adjusted	37	–
Hypertension, %	50	34
Diabetes, %	15	13
Median $eGFR_{CG}$, mL/min	43	60
Median $eGFR_{CKD\text{-}EPI,sCr}$, mL/min/1.73 m^2*	45	58
Median $eGFR_{CKD\text{-}EPI,cysC}$, mL/min/1.73 m^2†	57	77
Dipstick proteinuria, %	44	27
1+	29	20
2-3+	15	7
Significant proteinuria (UPCR >200 mg/g), %	56	35
Significant albuminuria (UACR ≥30 mg/g), %	64	42

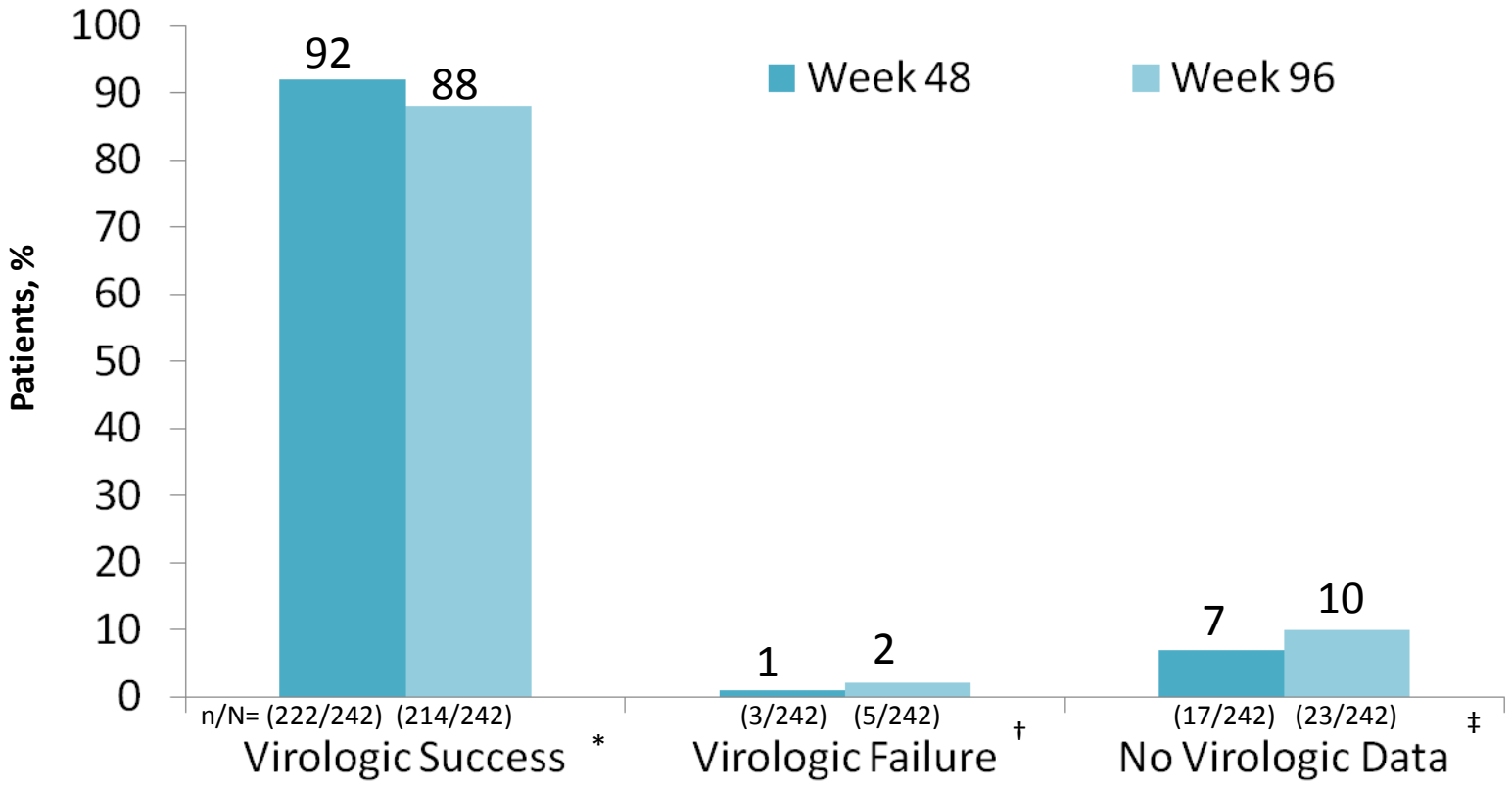




*Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation using serum creatinine (sCr; adjusted for age, sex, and race); †CKD-EPI equation using Cystatin C (CysC; adjusted for age and sex). UACR, urine albumin:Cr; UPCR, urine protein:Cr; ‡Some regimens included >1 third agent; therefore, total percentage >100%.

1. Post F, et al. CROI 2016. Boston MA. #680
2. Pozniak A, et al. JAIDS 2016;71(5):530-7

Virologic Outcomes at Week 96



E/C/F/TAF maintained high rate of virologic suppression at Week 96

*HIV-1 RNA<50 copies/mL; †HIV-1 RNA ≥50 copies/mL at Week 96 (n=2), discontinued due to lack of efficacy (n=2), took additional antiretroviral medications (n=1); ‡13 subjects discontinued due to adverse events; 10 subjects discontinued for other reasons (lost to follow-up, noncompliance, protocol violation) and last available HIV-1 RNA <50 copies/mL

1. Post F, et al. CROI 2016. Boston MA. #680
2. Pozniak A, et al. CROI 2015. Seattle, WA. #795
3. Gupta S, et al. ICAAC 2015. San Diego, CA. Oral
4. Pozniak A, et al. JAIDS 2016;71(5):530-7

Safety Summary

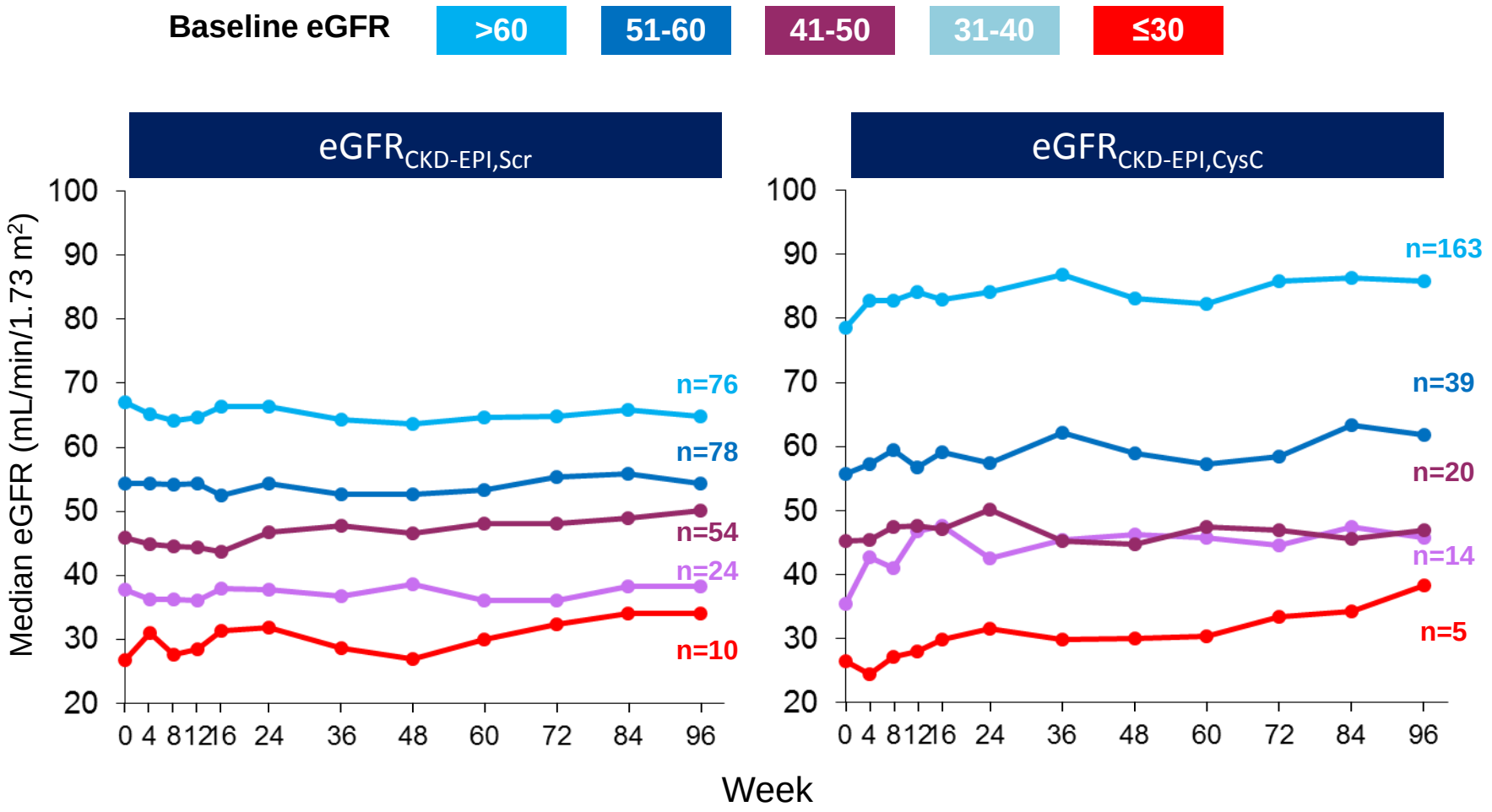
Safety Summary, n (%)	E/C/F/TAF N=242
Discontinuations due to Adverse Events (AEs)	12 (5)
Non-Renal AEs	7 (3*)
Decreased eGFR	5 (2†)
Most Common AEs, %	
Upper respiratory tract infection	14
Diarrhea	13
Arthralgia	12

*Diarrhea, malignant lung neoplasm, choking, dry mouth/fatigue/pruritis, joint swelling, sleep disorder, bladder transitional cell carcinoma
† 3 of 5 patients experienced renal disease progression (rising SCr on therapy; 2 of 3 also had poorly controlled hypertension)

- Regardless of baseline eGFR subgroup (< vs ≥ 50 mL/min) frequencies of adverse events and Graded AEs (1-4) were similar
- No patients developed renal tubulopathy or Fanconi's syndrome
  - Two patients with a medical history of TDF-associated Fanconi's syndrome remained on treatment with E/C/F/TAF with stable GFR, and significant reductions in total and tubular proteinuria

1. Post F, et al. CROI 2016. Boston MA. #680
2. Pozniak A, et al. JAIDS 2016;71(5):530-7

Changes in eGFR by Baseline eGFR Strata



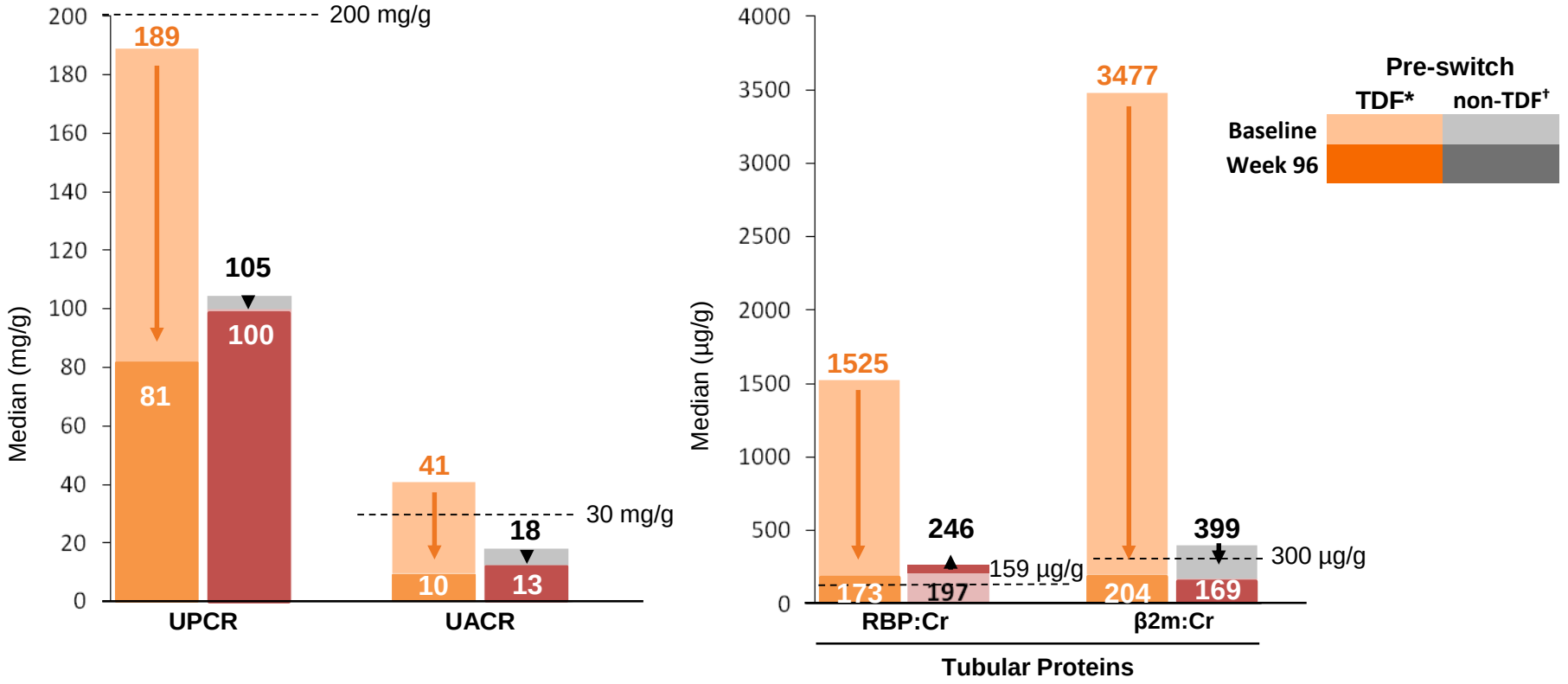
- N=5/242 (2%) discontinued study drug for decreased GFR
  - None with evidence of tenofovir associated tubulopathy

One patient was excluded due to missing CysC data at baseline.

1. Post F, et al. CROI 2016. Boston MA. #680
2. Pozniak A, et al. JAIDS 2016;71(5):530-7

Study 112: Suppressed Adults with Renal Impairment Switched to E/C/F/TAF (Week 96)

Renal Biomarkers: Changes From Baseline to Week 96



For all 4 proteinuria measures:

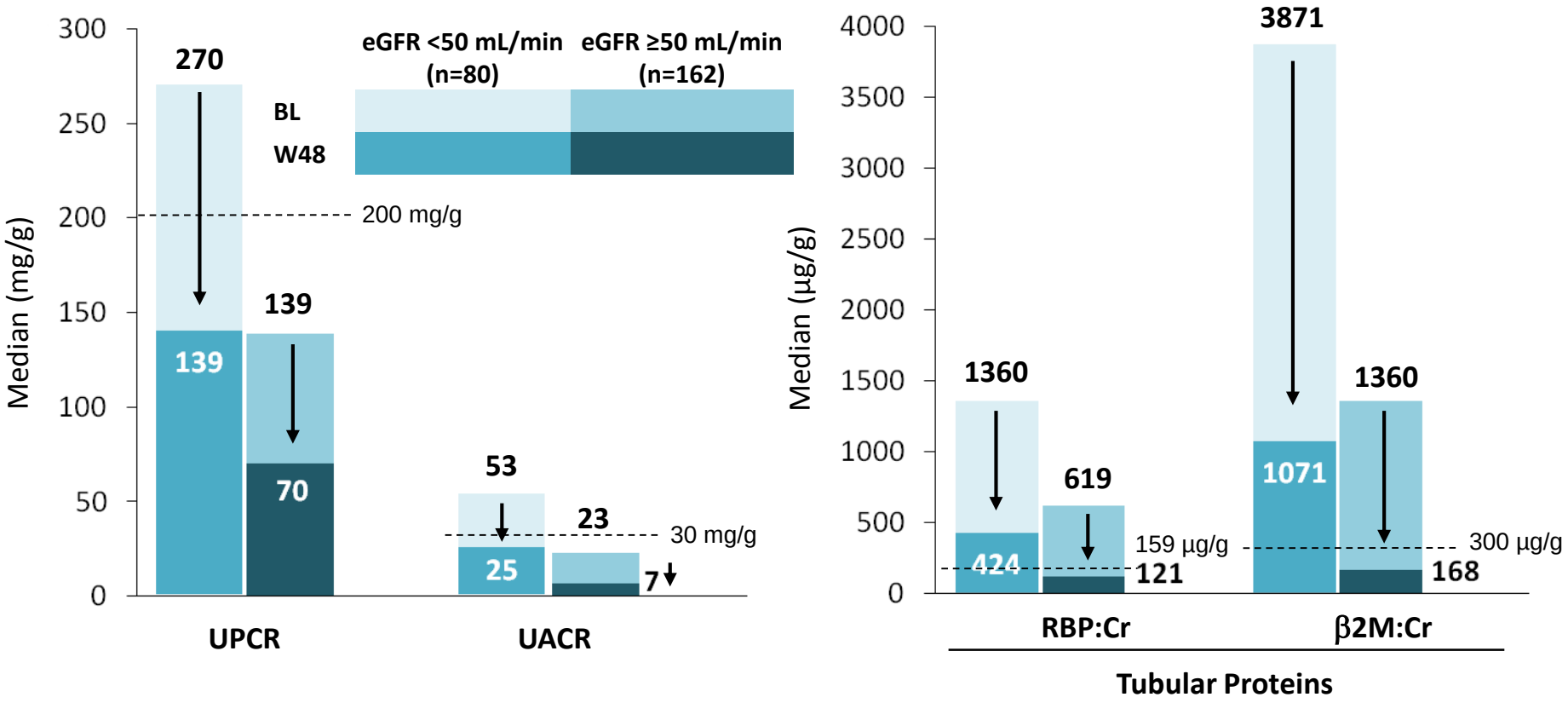
- Pre-switch TDF regimens were associated with elevations vs. non-TDF regimens
- Significant decreases observed with switch from TDF to TAF regimens
- Week 96 values were similar to baseline values with non-TDF regimens
- Minimal impact observed with switch from non-TDF to TAF regimens

* All changes statistically significant; †All changes not statistically significant with exception of β2m:Cr. β2m, β2-microglobulin; RBP, retinol-binding protein.

Post F, et al. CROI 2016. Boston, MA. Poster #680.

Study 112: Renal Impairment in Adults: Sub-Group Analysis by eGFR

Quantitative Proteinuria at BL and Week 48*



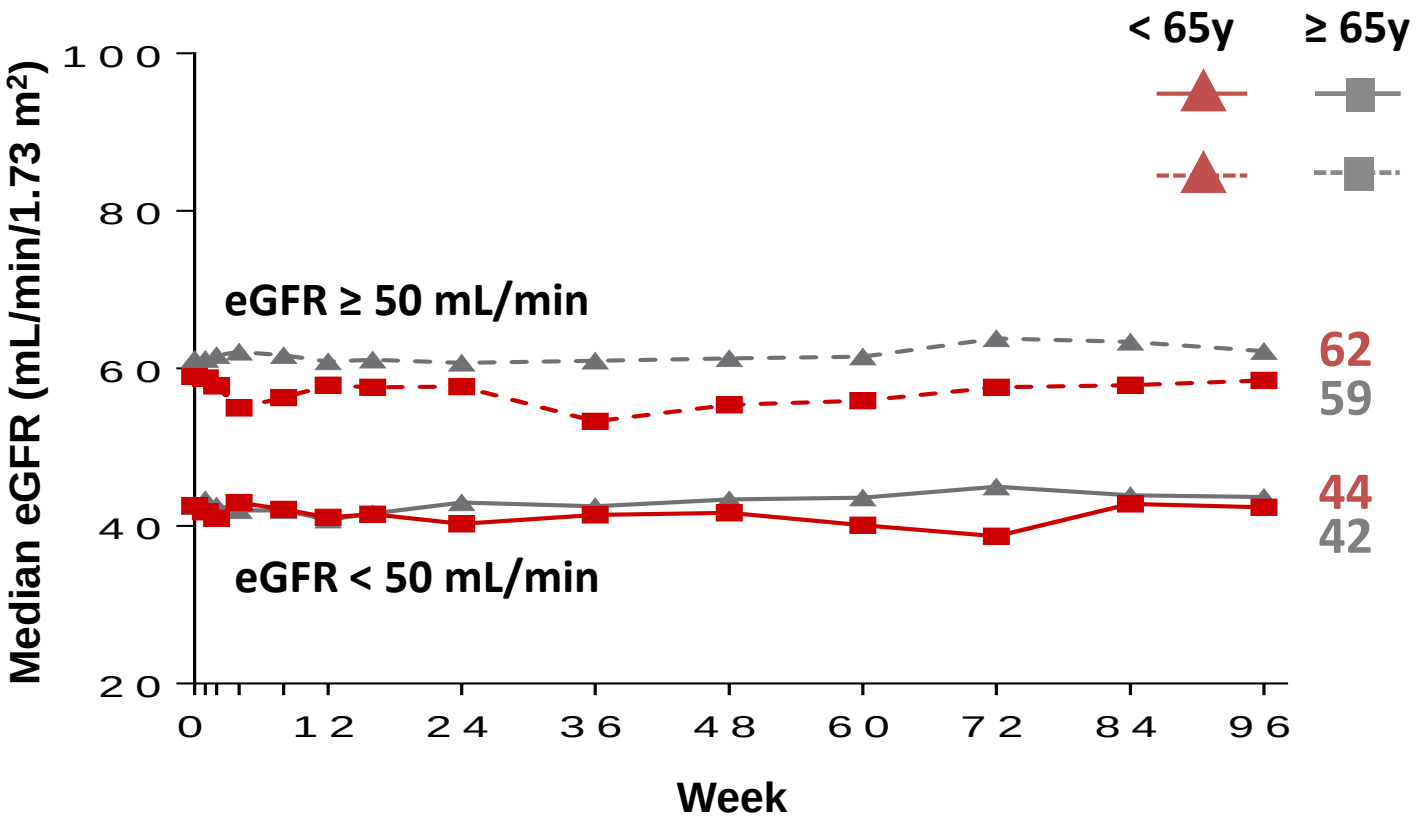
Significant decreases in multiple measures of proteinuria (low and high BL eGFR)

*P < 0.05 for all changes except β2M:Cr for 30-49 mL/min.

UPCR = Urine Protein:Creatinine Ratio; UACR = Urine Albumin: Creatinine Ratio
RBP:Cr = Retinol Binding Protein: Creatinine Ratio; β2M:Cr = β-2-microglobulin:Creatinine Ratio

Gupta S, et al. ICAAC 2015. San Diego, CA. Oral presentation

Median Changes in $eGFR_{CKD\text{-}EPI,Scr}$ by Age



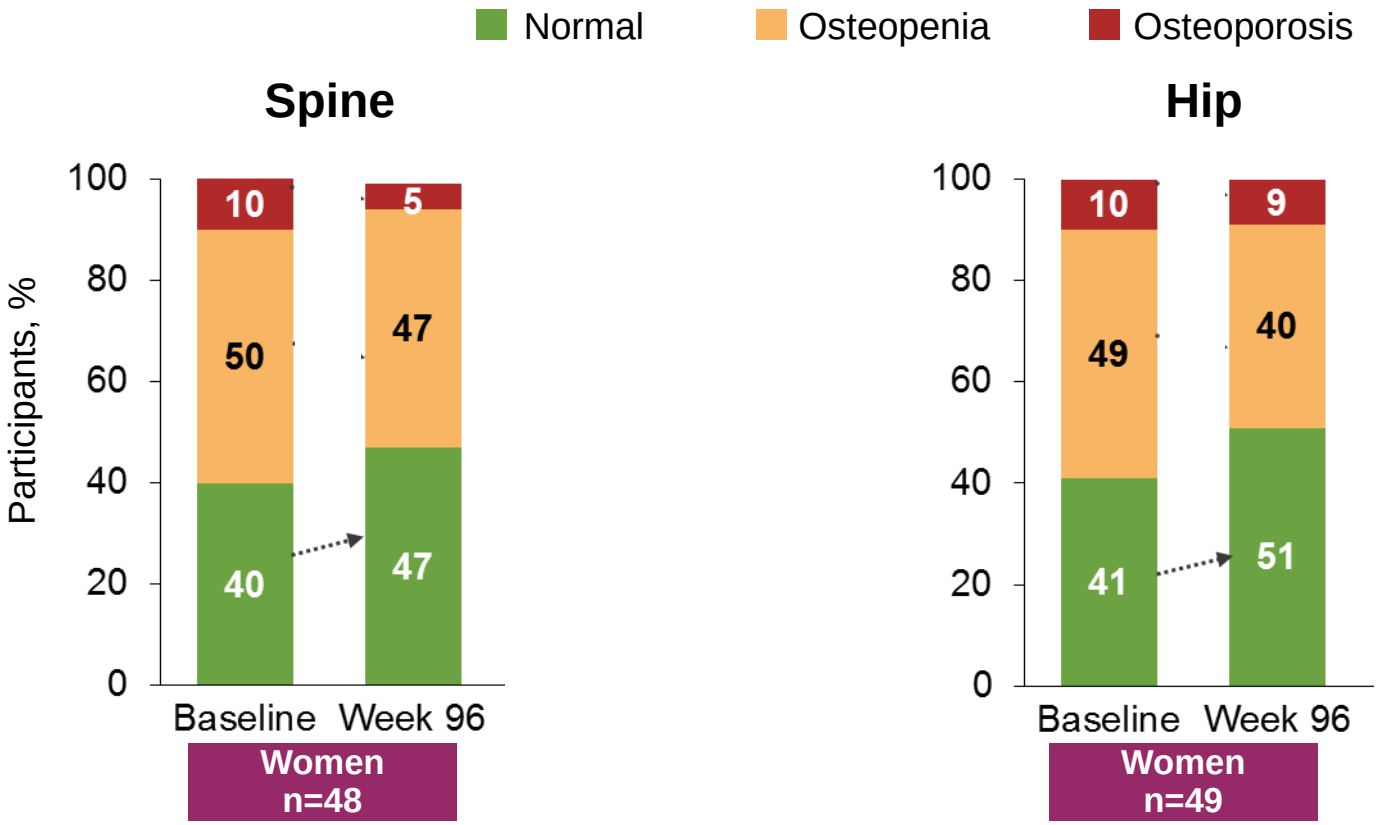
Regardless of baseline eGFR strata, eGFR remain stable over 96 weeks after switching to E/C/F/TAF in both age groups

$eGFR_{CKD\text{-}EPI,Scr}$: estimated glomerular filtration rate calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation using serum creatinine (sCr; adjusted for age, sex, and race)

Martorell C, et al. HIV and Aging 2016. Washington, DC. Poster #36

Study 112: Suppressed Women with Renal Impairment Switched to E/C/F/TAF

Change in Diagnosis of Osteopenia or Osteoporosis* through Week 96



Increase in the prevalence of normal BMD and decrease in osteopenia/osteoporosis

* Osteopenia and osteoporosis as defined by T-score

McDonald C, et al. ASM 2016. Boston MA. Oral

Outcomes in Subjects with Low Baseline BMD Switched from TDF to TAF

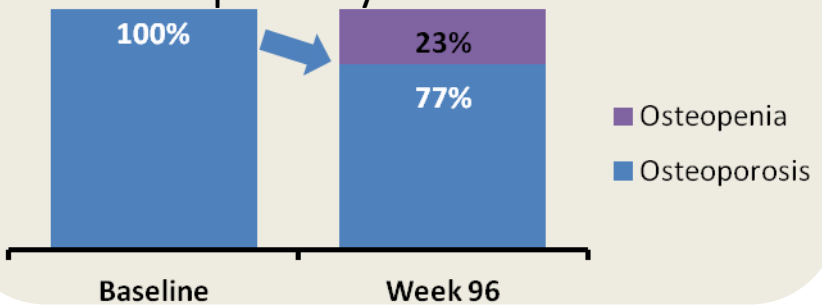
Analysis of outcomes and predictors of clinically significant BMD increases (≥5%) at W96 in the 214 subjects with low baseline BMD (T-score ≤ -2.0) in pooled TAF studies (E/C/F/TAF Studies 109 and 112)

Baseline T-score ≤ -2.0

- Significant BMD increases observed
  - Spine: +2.53% (p<0.001)
  - Hip: +2.39% (p<0.001)
- Proportion of low BMD participants experiencing ≥5% BMD increase
  - Spine: 27% (52/193)
  - Hip: 16% (32/195)

Baseline T-score ≤ -2.5

- 86 subjects with low baseline BMD also had osteoporosis*
  - 23% of these subjects improved to osteopenia by Week 96



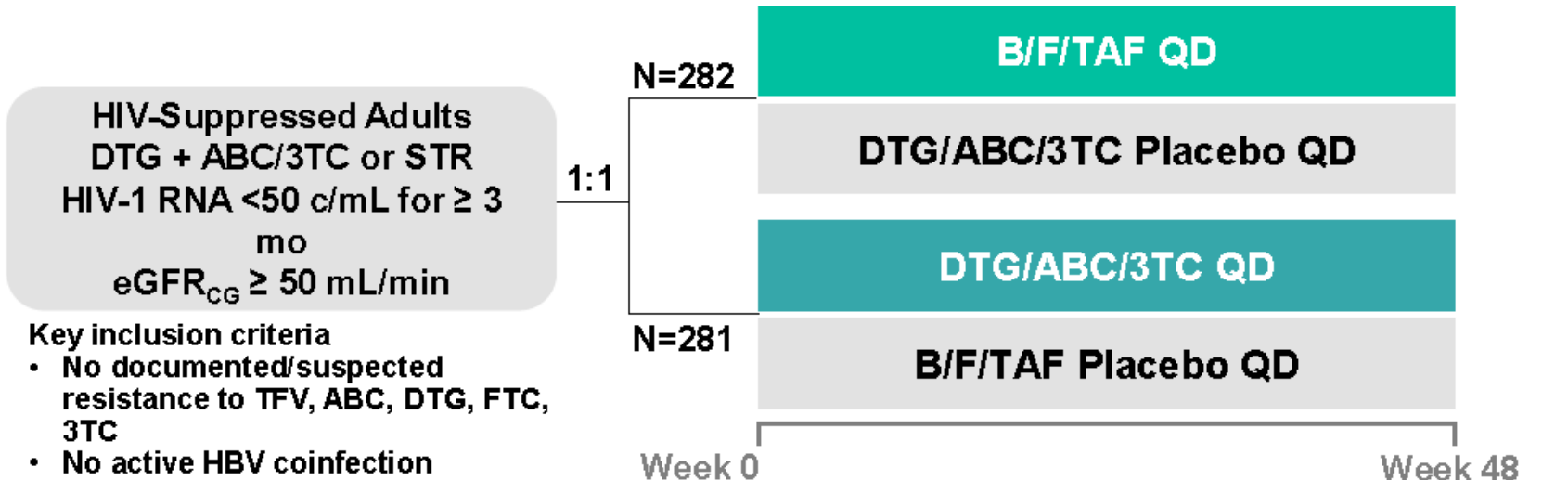
- Factors predicting ≥5% BMD increase after a switch from TDF to TAF:
  - Urinary phosphate wasting ($FEPO_4$ ≥ 10%) or
  - High bone turnover (P1NP levels >1.72 $\log_{10}$ ng/mL)

* Subjects had osteoporosis at baseline and W96 follow-up BMD data

Brown T, et al. CROI 2017. Seattle, WA. Poster #683

Study Design

Phase 3, multicenter, randomized, double-blind, active-controlled study



Key inclusion criteria
- No documented/suspected resistance to TFV, ABC, DTG, FTC, 3TC
- No active HBV coinfection
- HCV coinfection allowed[2]

Study sites: North America, Europe, Australia

ClinicalTrials.gov Identifier: NCT02603120

Primary Endpoint

- HIV-1 RNA ≥50 copies/mL at Week 48 by FDA-defined snapshot algorithm (4% non-inferiority margin)

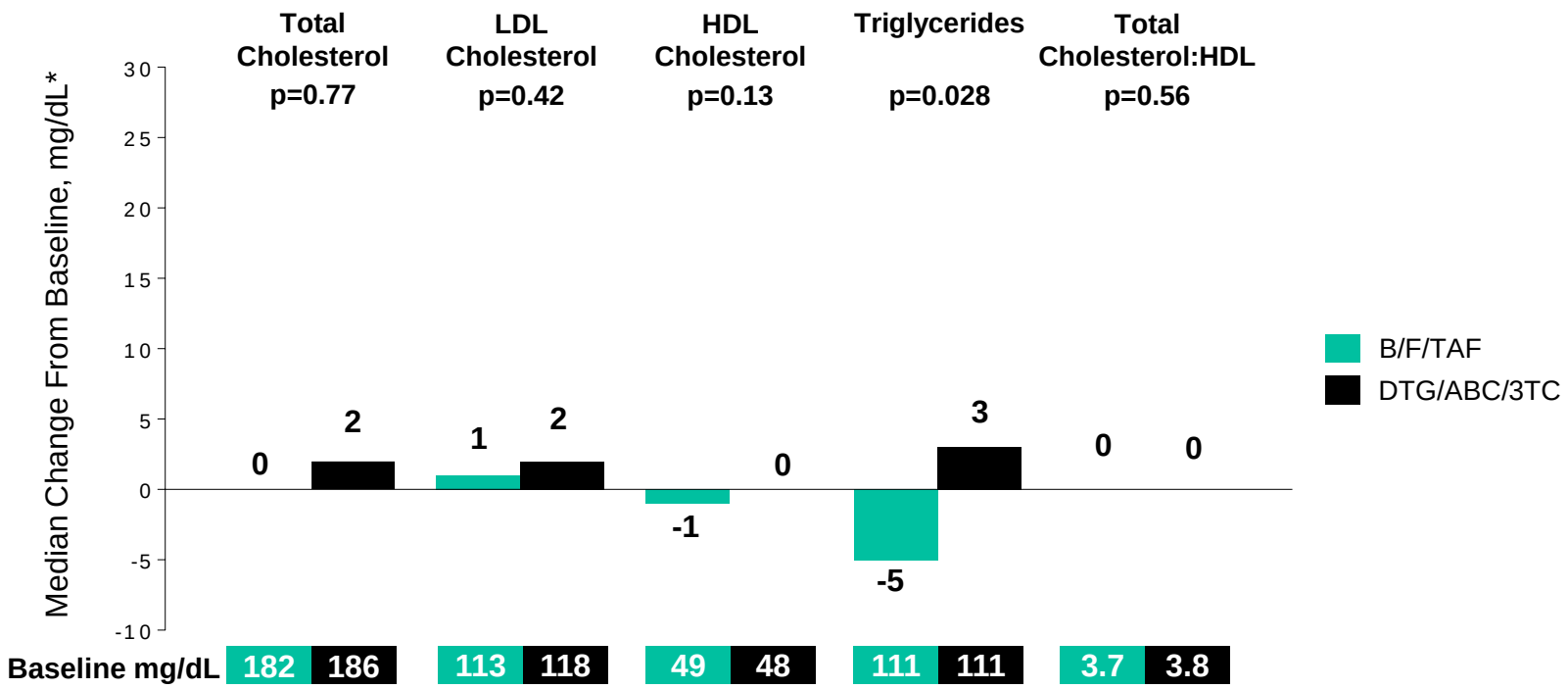
Secondary Endpoint

- HIV-1 RNA <50 copies/mL at Week 48[3]

eGFRCG, estimated glomerular filtration rate by Cockcroft-Gault

1. Molina JM, et al. CROI 2018. Boston, MA. Oral 22.
2. Gilead Sciences. Data on File.
3. ClinicalTrials.gov URL: https://clinicaltrials.gov/ct2/show/NCT02603120 Accessed on March 5, 2018
4. Andreatta K, et al. CROI 2018. Boston, MA. Poster 506

Fasting Lipid Changes at Week 48



*p-values from 2-sided Wilcoxon rank-sum test

Stellbrink et al, HIV Glasgow 2018 #O211

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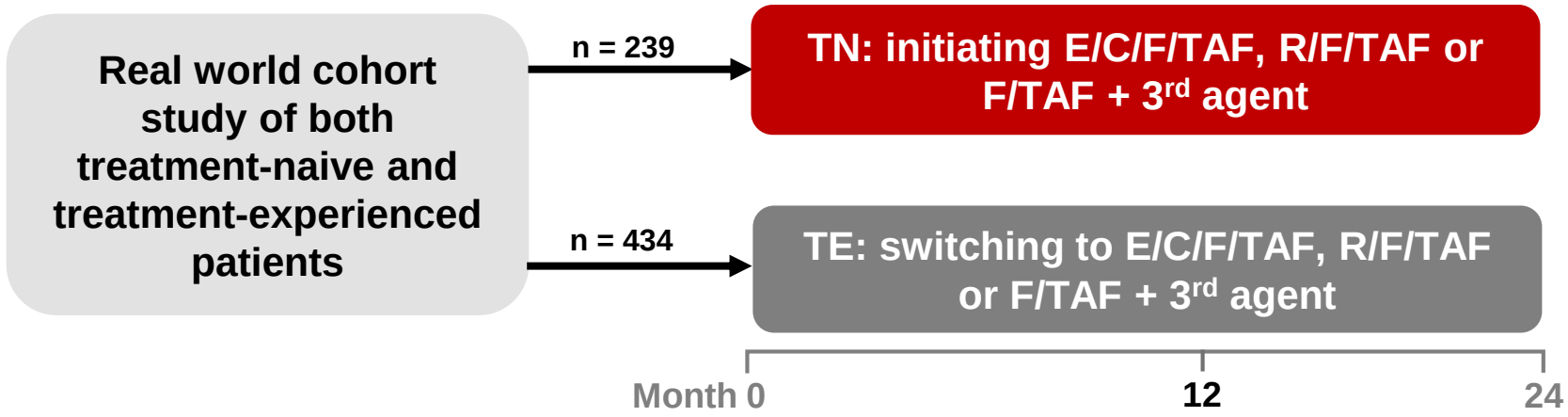
Effectiveness, Persistence & Safety of F/TAF-based regimens

Non-interventional 24-month prospective cohort study



Outcome Measures

- ART persistence (using Kaplan-Meier analyses)
- Virologic effectiveness (HIV-RNA<50 cp/mL using modified ITT-analyses [mITT], discontinuation=failure, loss-to-follow-up and missing=excluded)
- Incident serious/non-serious adverse drug reactions (SADRs/ADRs) and health-related quality of life (HRQL) using validated questionnaires (SF-36, HIV Symptom Index)

1. Heuchel T, et al. HIV Glasgow 2018. Poster P05; 2. Hillenbrand H, et al. HIV Glasgow 2018. Poster P069

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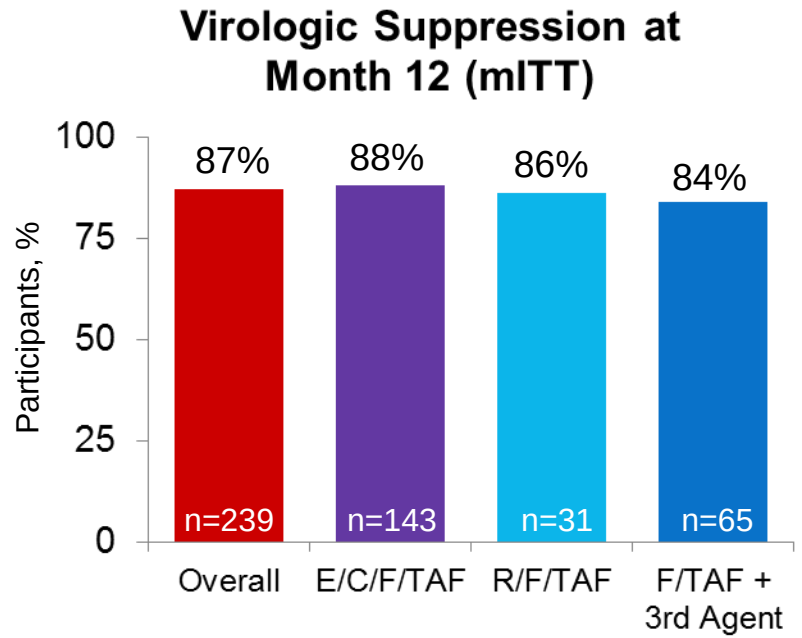
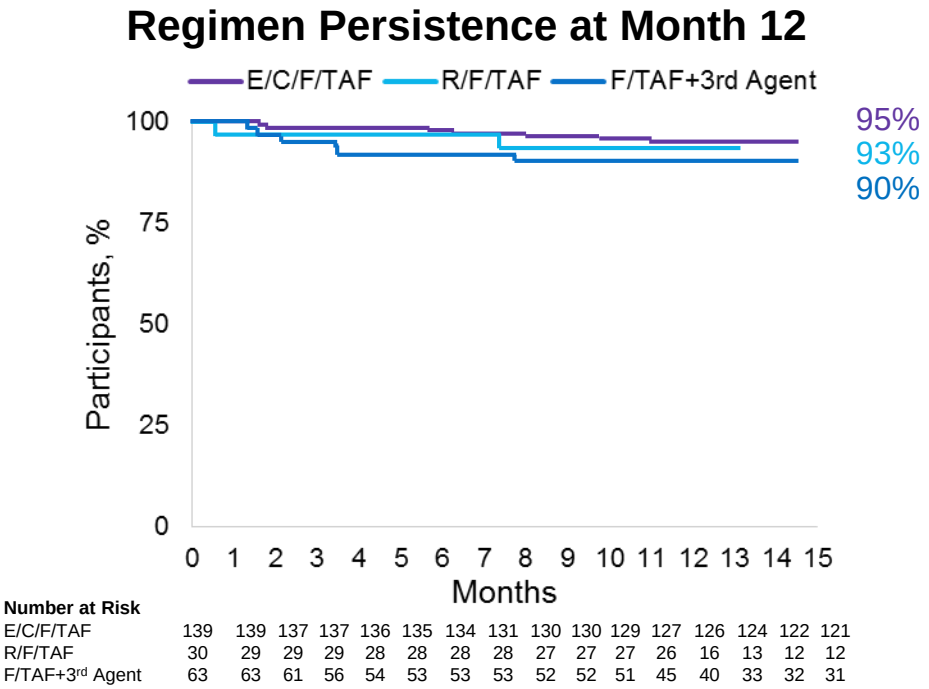
Results: Treatment-naive patients





- F/TAF-based regimens for initial ART showed good persistence with >90% through 12 months in this prospective cohort of treatment-naïve adults
- Low discontinuation rates due to ADRs (<2%)
- VF = 1% [n=2; E/C/F/TAF (n=1), R/F/TAF (n=1)]

Heuchel T, et al. HIV Glasgow 2018. Poster P052

‡

Baseline characteristics: Treatment-experienced patients

	Overall*
N (%)	434 (100)
Male gender, n (%)	393 (91)
Age, years, median (IQR)	51 (40-57)
Age ≥50 years, n (%)	251 (58)
HIV-related characteristics	
CD4 count, cells/µL, median (IQR)	629 (472-831)
CDC stage C (AIDS), n (%)	90 (21)
HIV-1 RNA (cp/mL)	
<50, n (%)	405 (95)
50 - <200, n (%)	13 (3)
200 - 100,000, n (%)	6 (1)
>100,000, n (%)	1 (<1)
Previous antiretroviral regimen, n (%)	
INI-based	153 (35)
NNRTI-based	164 (38)
PI-based	75 (17)
Other	42 (10)
TDF-based regimen	93%

*Calculations are based on observed data; IQRm interquartile range; **inclusion criteria for this group age ≥50 years

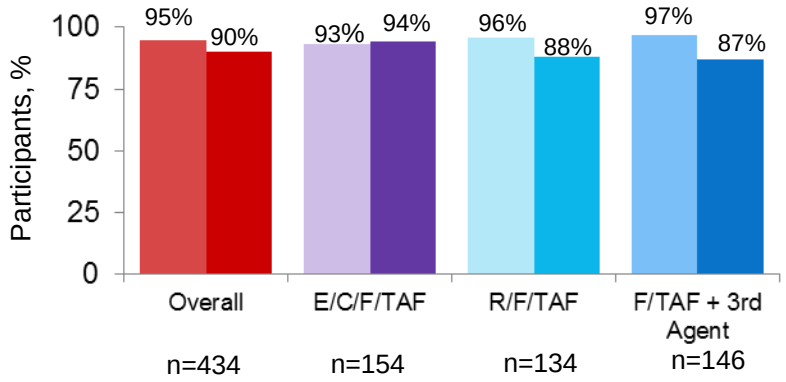
Hillenbrand H, et al. HIV Glasgow 2018. Poster P069

‡

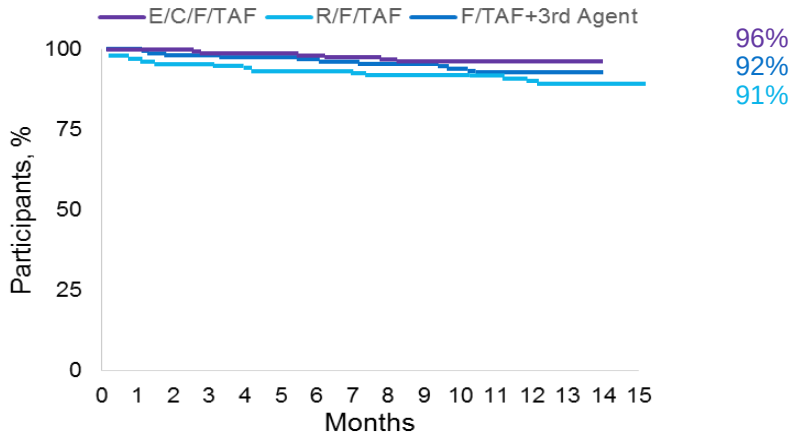
Results: Treatment-experienced patients

- Reasons for switch included simplification (29%), patient request (32%), side effects on current ART (43%) and other (18%)

Virologic Suppression at Baseline and Month 12 (mITT)



Regimen Persistence at Month 12



Reasons for study and/or study drug discontinuation, n (%)	Overall	E/C/F/TAF	F/TAF + 3rd agent	R/F/TAF
ADRs	9 (2)	3 (2)	1 (1)	5 (4)
Patient decision	6 (1)	1 (1)	3 (2)	2 (1)
Virologic failure (VF)	3* (1)	1† (1)	0 (0)	2 ‡ (1)
Death	2** (<1)	0 (0)	1 (1)	1 (1)
Other	9 (2)	1 (1)	6 (4)	2 (1)
Loss to follow-up	6 (1)	4 (3)	0 (0)	2 (1)

- Significant improvements in treatment satisfaction: Total score (overall) = +15.8, p <0.05, [-30; +30], also demonstrated in subgroups (p<0.05)

*All with <50 cp/mL at baseline; † 1 patient without baseline (BL) resistance test, but with multiple resistance associated mutations (RAMs) at VF including NNRTI mutations and thymidine analogue mutations (TAMs) indication for historic failure (previous ART: DTG+F/TDF); ‡ 1 patient without BL resistance test and no resistance mutations at VF (previous ART R/F/TDF), 1 patient without BL RAMS but RAMs at VF including TAMs (previous ART: DRV/r + F/TDF); **causes of death: 1 x esophageal variceal bleeding, 1 x unknown

Hillenbrand H, et al. HIV Glasgow 2018. Poster P069

‡

Demographics and medical characteristics of the patients

	All switched (n=84)	eGFR at the time of switch subgroups		P values*
		≥ 90 mL/min/1.73m² (n=41)	<90 mL/min/1.73m² (n=43)	
Gender; male, n (%)	78 (92.9)	37 (90.2%)	41 (95.3%)	0.374
At time of switch				
Age (year); median (IQR)	40 (34 – 52)	38 (33 – 45)	44 (36 – 54)	0.014
Age >50 years, n (%)	23 (27.4)	7 (17.1%)	16 (37.2%)	
HIV RNA <50 copies/mm³; n (%)	79 (94.0)	38 (92.7%)	41 (95.4%)	
Previous E/C/F/TDF usage duration; month, median (IQR)	24 (12 – 36)	24 (12 – 36)	36 (24 – 48)	0.034
At the time of diagnosis				
CD4 T-lymphocyte > 500 cells/mm³; n (%)	24 (28.6)	14 (34.1)	10 (23.3)	
CD4 T-lymphocyte <200 cells/mm³; n (%)	20 (23.8)	6 (14.6)	14 (32.6)	

IQR: interquartile range
* P values from univariate comparison; an additional logistic regression model using backward selection of gender, age, log(CD4 T-lymphocyte count), log (HIV RNA) and previous E/C/F/TDF usage duration revealed that patients with baseline eGFR≥ 90 mL/min/1.73m² were younger (odds ratio [95%CI]: 0.95 [0.90 - 0.99], P=0.018) and had been significantly less time on TDF (odds ratio [95%CI]: 0.98 [0.95 - 0.99], P=0.034) than patients with baseline eGFR <90 mL/min/1.73m²

Rieke AH, et al. HIV Glasgow 2018. Poster P206

‡

Unadjusted eGFR increased significantly from time of switch to month 12

Unadjusted eGFR over time in patients with data from the time of switch to month 12

	median (IQR)	P*
All switched (n=66)		
At the time of the switch	86.2 (75.3 – 98.9)	
Month 3	91.1 (81.9 -100.7)	0.148
Month 6	88.1 (77.7 - 100.4)	0.518
Month 12	94.7 (81.7 - 103.7)	0.004
eGFR at the time of switch ≥ 90 mL/min/1.73m² (n=28)		
At the time of the switch	103.4 (97.2 - 111.0)	
Month 3	101.1 (97.6 - 111.6)	0.806
Month 6	100.1 (92.9 - 110.1)	0.399
Month 12	102.1 (97.2 - 116.9)	0.857
eGFR at the time of switch < 90 mL/min/1.73m² (n=38)		
At the time of the switch	77.0 (67.9 - 83.3)	
Month 3	84.4 (74.5 - 90.8)	0.002
Month 6	81.7 (73.0 - 88.7)	0.021
Month 12	84.3 (74.07 - 95.0)	0.001

eGFR: estimated glomerular filtration rates; IQR: interquartile range
* P values are for the comparison between each time point and the time of switch by using univariate Wilcoxon signed-rank test

Rieke AH, et al. HIV Glasgow 2018. Poster P206

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EVOLUTION AND REVERSIBILITY OF RENAL FUNCTION AFTER SWITCH FROM TDF TO TAF REGIMENS

Roberta Gagliardini[1] Patrizia Lorenzini[1], Alessandro Cozzi-Lepri[2], Nicola Gianotti[3], Loredana Sarmati[4], Stefano Rusconi[5], Emanuela Messina[3], Amedeo Capetti[5], Annalisa Saracino[6], Giordano Madeddu[7], Antonella D'Arminio Monforte[8], Andrea Antinori[1], for the Icona Foundation Study Group

[1]Istituto Spallanzani National Institute for Infectious Diseases IRCCS, Rome, Italy; [2]University College London, London, UK; [3]San Raffaele Scientific Institute, Milan, Italy; [4]University of Rome Tor Vergata, Rome, Italy; [5]ASST Fatebenefratelli, Milan, Italy; [6]University of Siena, Siena, Italy; [7]University of Sassari, Sassari, Italy; [8]University of Milan, Milan, Italy

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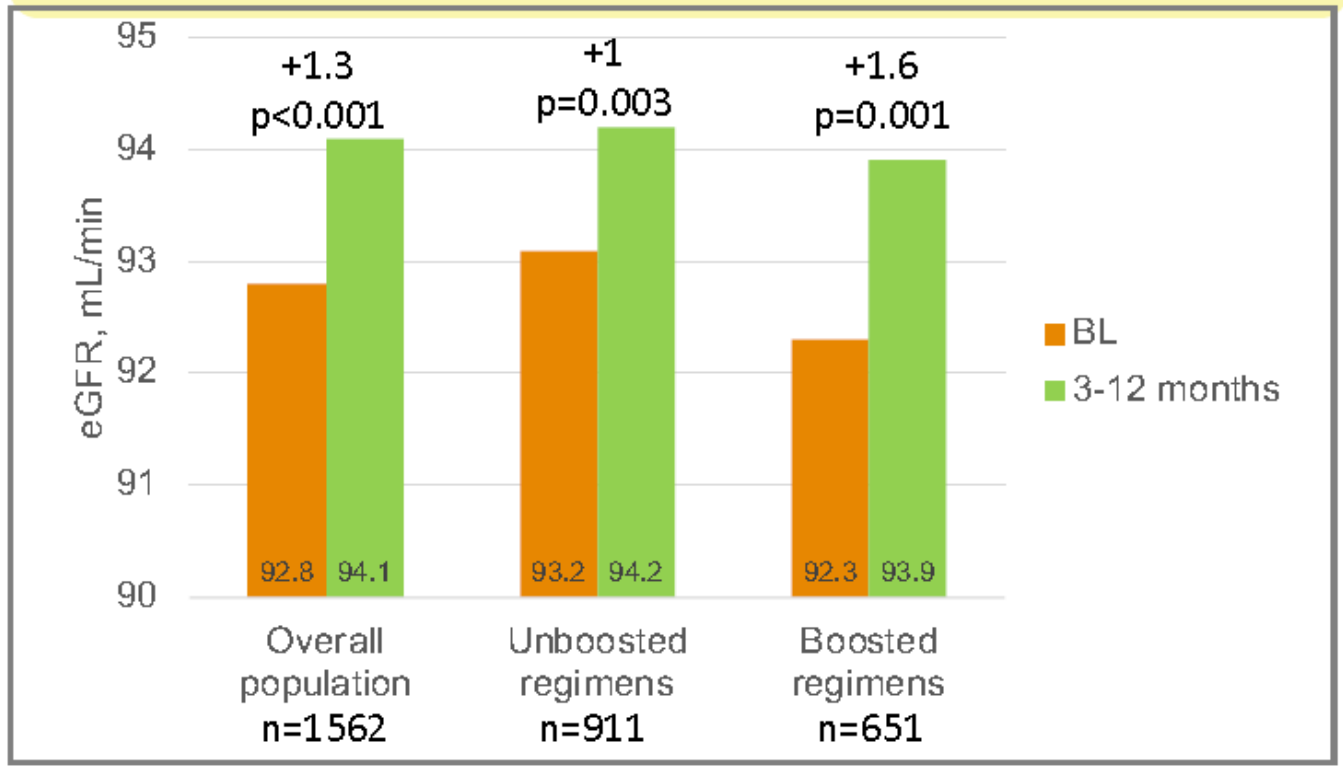
Seattle March 4–7, 2019

Figure 2– Evolution of eGFR after 3-12 months post switch from TDF to TAF



No differences in mean changes of eGFR between the two groups were observed.

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[1]Lazzaro Spallanzani National Institute for Infectious Diseases INMI, Rome, Italy; [2]University College London, London, UK; [3]San Raffaele Scientific Institute, Milan, Italy; [4]University of Rome Tor Vergata, Rome, Italy; [5]ASST Fatebenefratelli, Milan, Italy; [6]University of Siena, Siena, Italy; [7]University of Sassari, Sassari, Italy; [8]University of Milan, Milan, Italy

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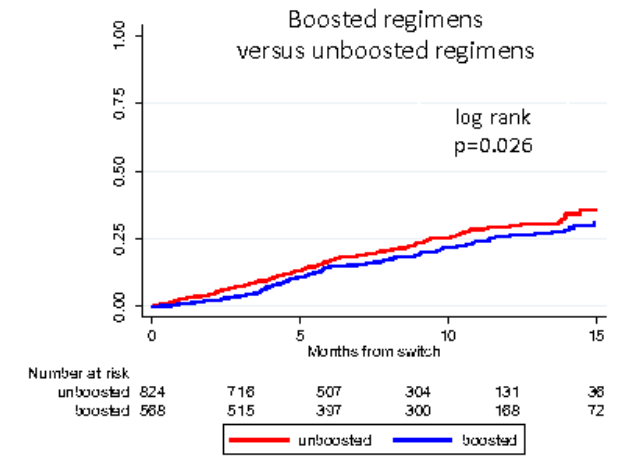
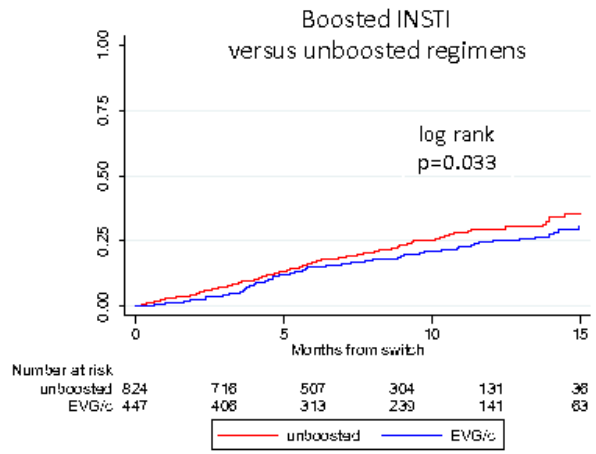
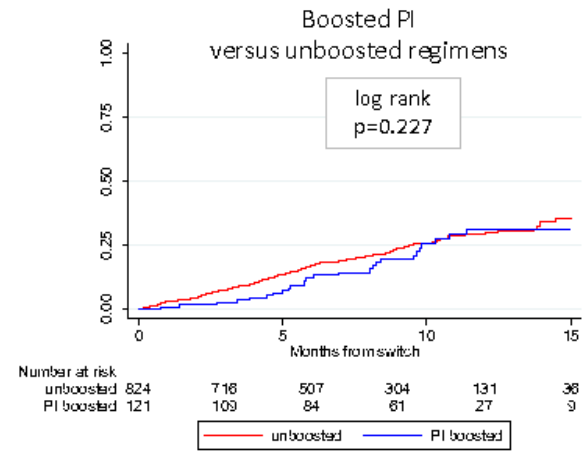
The estimated probabilities of **recovery of eGFR to pre-TDF values was slightly higher with unboosted regimens**, as shown in Figure 3.

Figure 3 – Estimated probabilities of recovery of eGFR to pre-TDF values







EVOLUTION AND REVERSIBILITY OF RENAL FUNCTION AFTER SWITCH FROM TDF TO TAF REGIMENS

Roberta Gagliardini[1] Patrizia Lorenzini[1], Alessandro Cozzi-Lepri[2], Nicola Gianotti[3], Loredana Sarmati[4], Stefano Rusconi[5], Emanuela Messina[3], Amedeo Capetti[5], Annalisa Saracino[6], Giordano Madeddu[7], Antonella D'Arminio Monforte[8], Andrea Antinori[1], for the Icona Foundation Study Group

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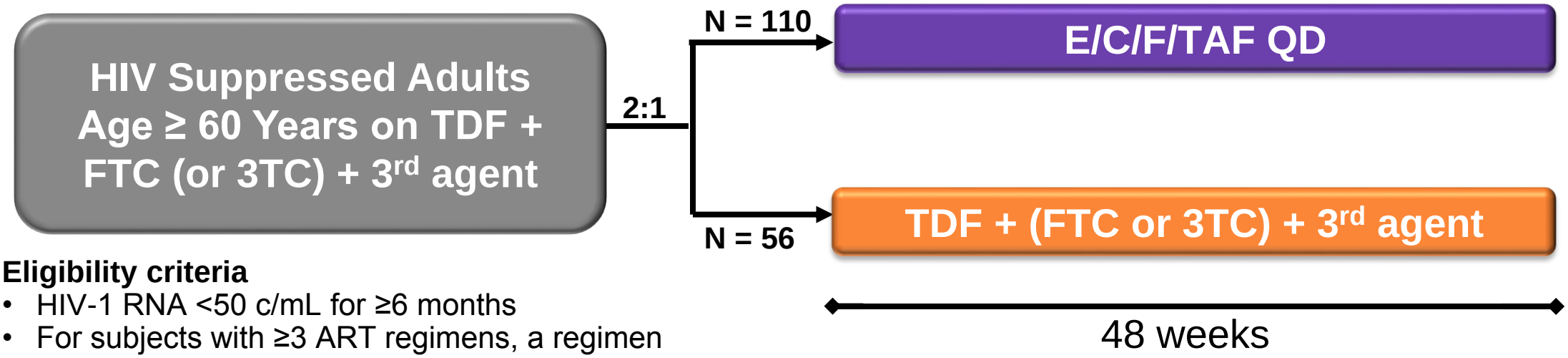
Table 2 – Predictors of eGFR recovery to pre-TDF values

	aIRR	95% CI	P value
CDC stage C	0.83	0.55- 1.25	0.365
Age (+10 years)	0.96	0.87- 1.06	0.427
Years of TDF exposure (+ 1 year)	**0.90**	**0.86- 0.94**	**<0.001**
Boosted vs unboosted regimen	**0.74**	**0.59- 0.92**	**0.008**

Notes: aIRR, adjusted incident rate ratio; CI, confidence intervals.
Variables explored in the model were: gender, age, mode of HIV transmission, ethnicity, years of HIV infection, HCV and HBV coinfection, nadir CD4, current CD4, current CD8, current HIV-RNA, duration of ART exposure, number of previous regimens, smoke habit, hypertension and diabetes.

Switch from TDF to E/C/F/TAF for Age ≥ 60

Multicenter, randomized, open-label, active control, 48-week study



Eligibility criteria

- HIV-1 RNA <50 c/mL for ≥6 months
- For subjects with ≥3 ART regimens, a regimen history must be reviewed

Primary Endpoint

- Mean percent change from Day 1 to Week 48 in spine and hip BMD by DXA

Secondary Endpoints

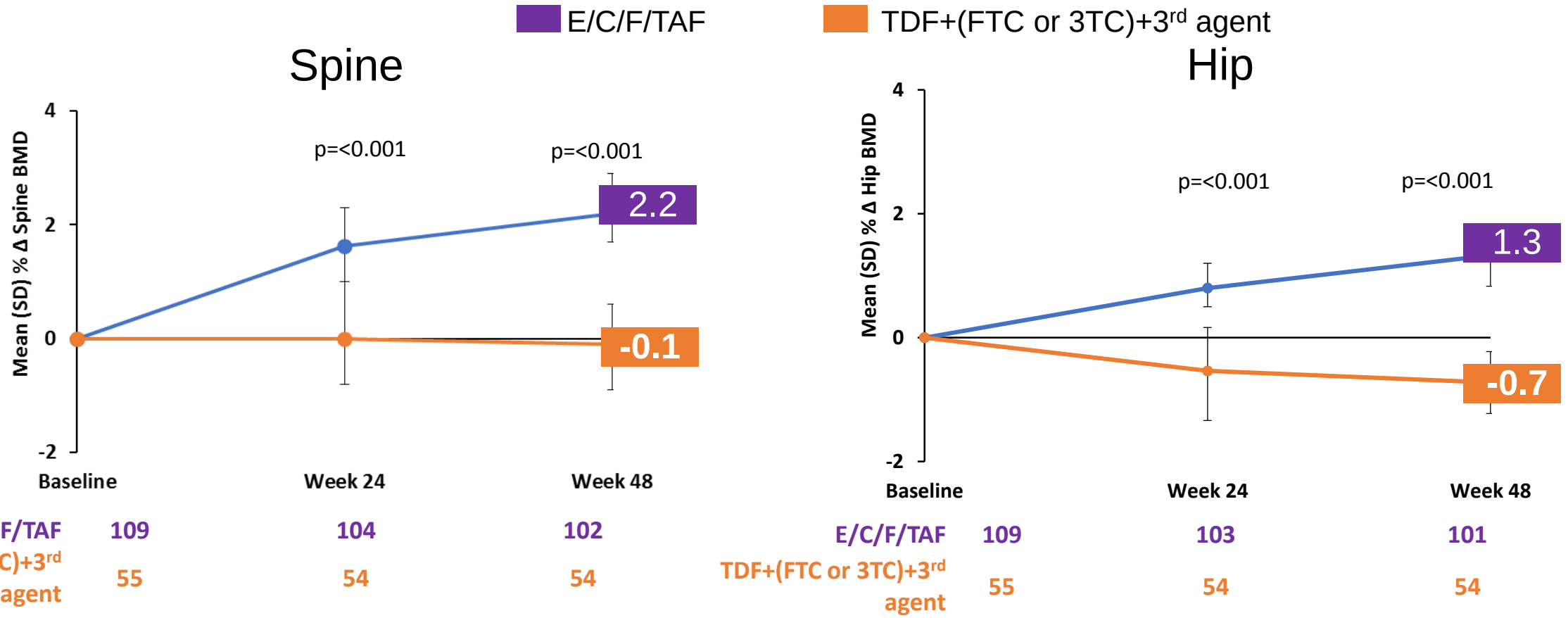
- Mean percent change from Day 1 to Week 24 in spine and hip BMD by DXA
- Safety profile: adverse events, clinical laboratory tests
- HIV RNA < 50 copies/ mL at Week 24 and 48 using FDA snapshot

Maggiolo F, et al. Glasgow 2018; Lancet HIV submitted

Baseline Characteristics

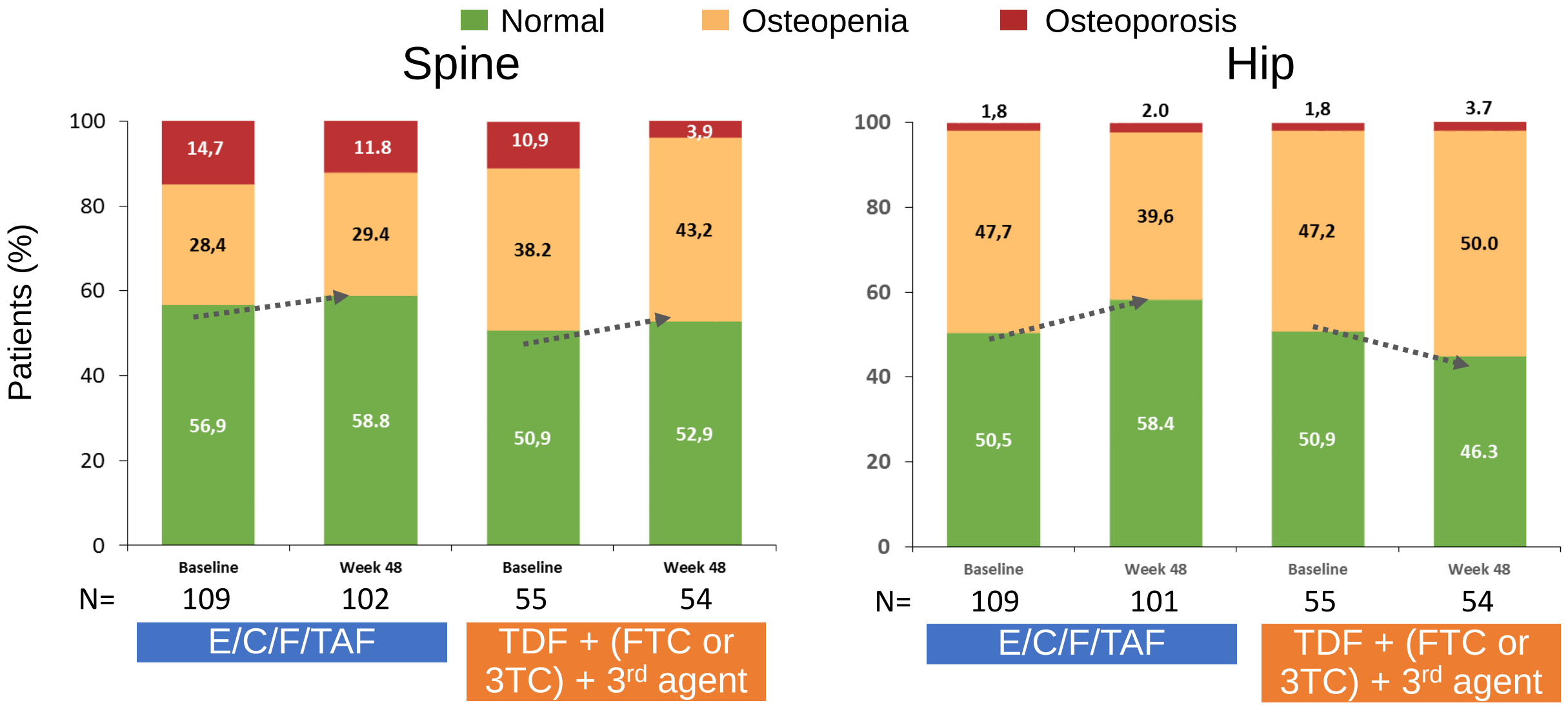
	E/C/F/TAF N=110	TDF + (FTC or 3TC) + 3rd agent N=56
Median age, years (range)	64 (60-80)	65 (60-80)
Female, % (n)	13% (14)	9% (5)
Race, %, (n)		
White	94% (103)	88% (49)
Median estimated GFR_{CG}, mL/min (range)	80 (46-165)	80 (46-124)
Mode of Infection		
MSM (n)	47% (52)	34% (19)
Heterosexual (n)	44% (48)	57% (32)
HIV RNA < 50 copies/mL at baseline	109 (99)	56 (100)
Median CD4 count, cells/mm^3, (range)	618 (231-1430)	667 (183-1516)
Baseline Regimen (n)		
NNRTI	73% (80)	73% (41)
INSTI	19% (21)	14% (8)

Change in Spine and Hip BMD Through Week 48

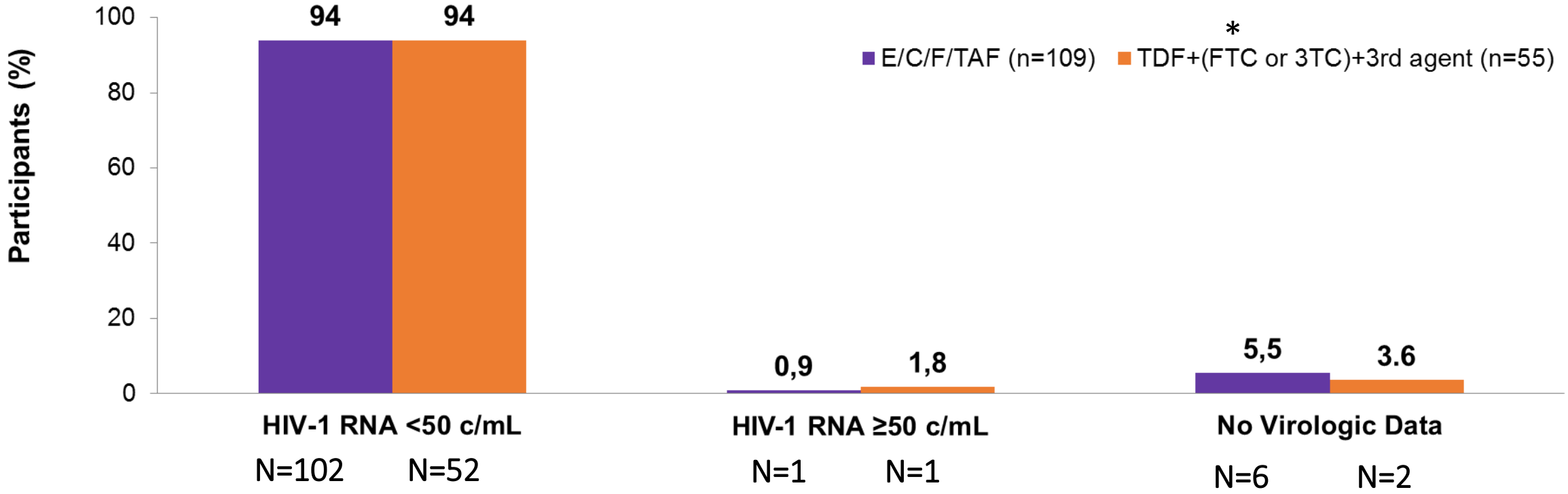


BMD=bone mineral density
P-values reflect comparison between visit and baseline

Change in Diagnosis of Osteopenia or Osteoporosis Defined by T-Score



Virologic Outcomes at Week 48 (Snapshot Analysis)



* One subject was excluded due to a disallowed regimen

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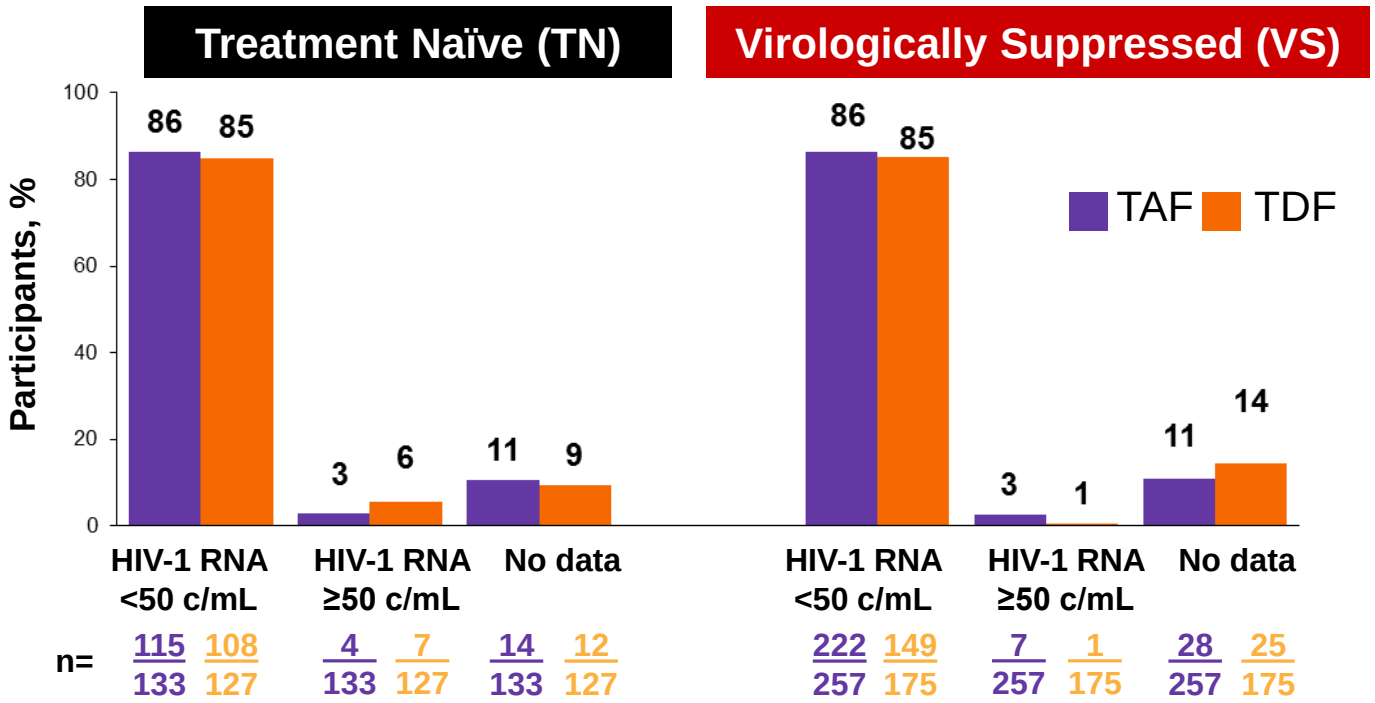
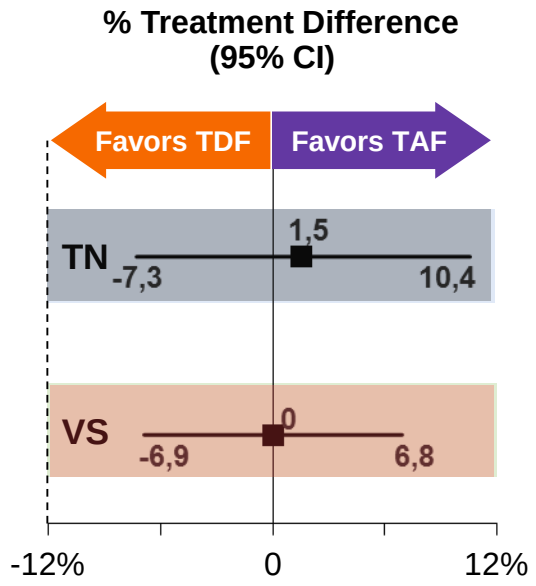
Virologic Outcomes at Week 96 in Women

Pooled analysis of 779 women from 7 randomized studies comparing TAF to TDF
(2 in treatment naïve women [n= 260] and 5 in virologically suppressed women [n=519])





Suppression Rates in Men (TAF vs TDF): TN: 87% vs 85%; VS: 91% vs 89%

Efficacy results were similar for TAF vs. TDF in both women and men

Thompson M, et al. CROI 2019. Seattle, WA. Poster 519

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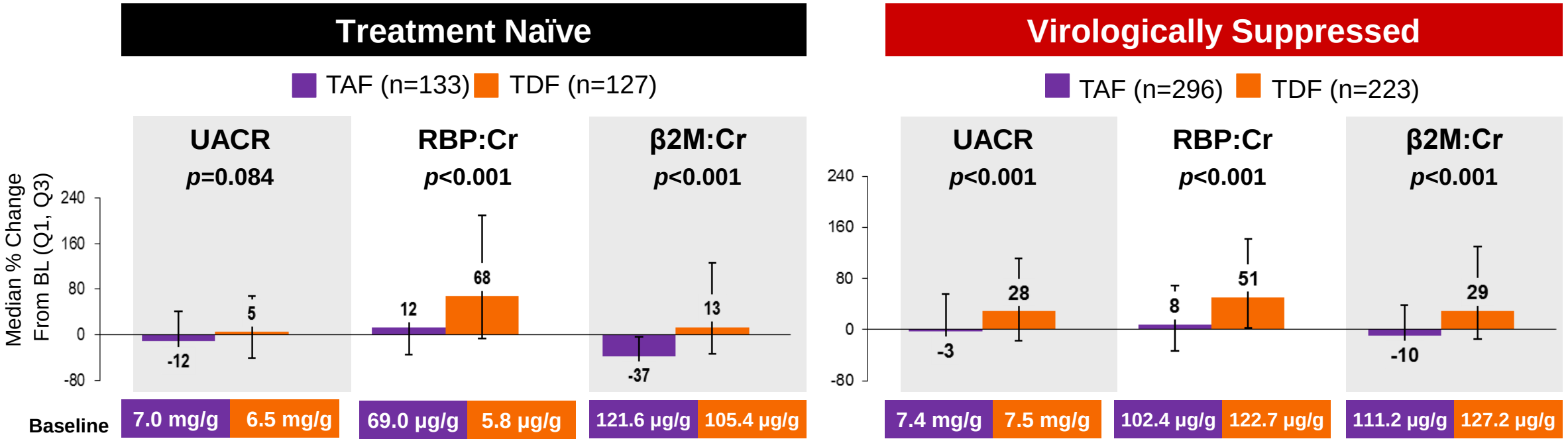
Changes in Renal Biomarkers at Week 96 in Women



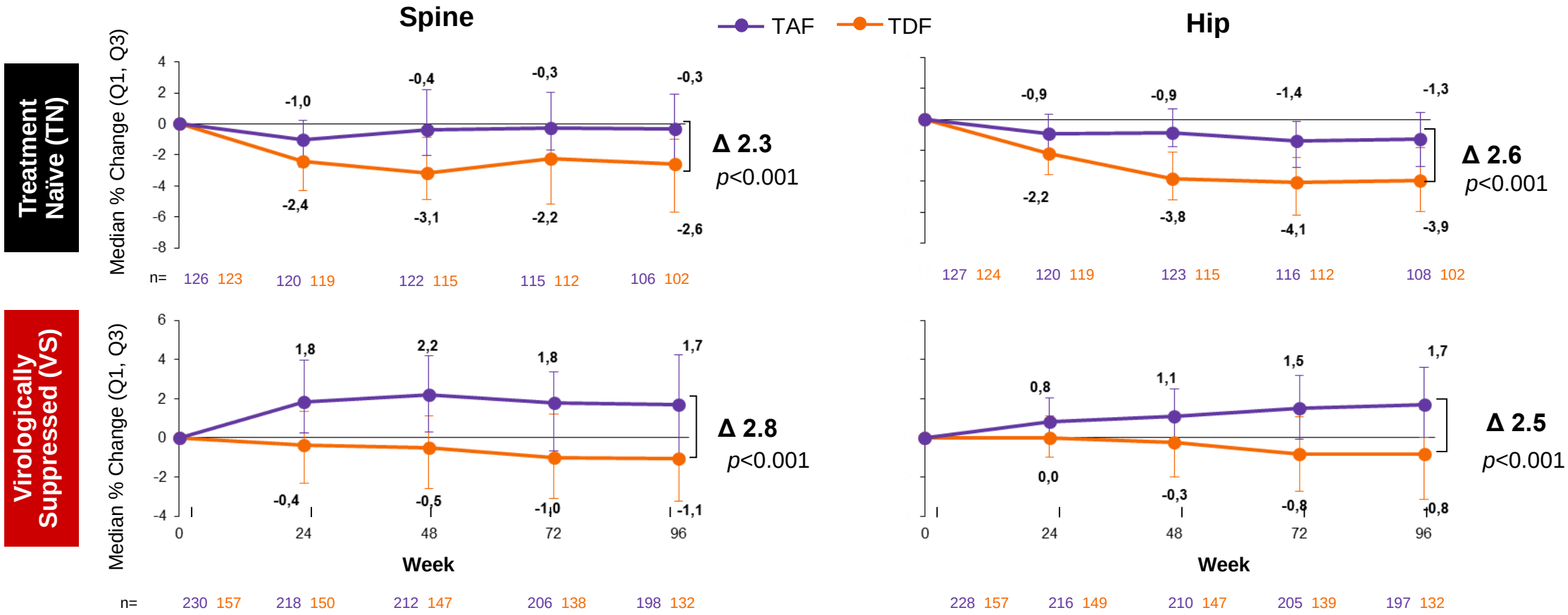
- Rates of treatment-emergent renal AEs in women were low
- No participant on TAF developed PRT

Women initiating or switching to TAF had less tubular proteinuria (RBP:Cr, β2M:Cr) vs. TDF. These results were similar to those in men.

ß2M, ß2 microglobulin; Cr, creatinine; RBP, retinol-binding protein; UACR, urine albumin:Cr ratio.

Thompson M, et al. CROI 2019. Seattle, WA. Poster 519

BMD Change through Week 96 in Women



Women initiating TAF had less BMD decline vs. TDF, and women switching to TAF from TDF had improvements in BMD. Results were similar to those in men.

Thompson M, et al. CROI 2019. Seattle, WA. Poster 519

TAKE HOME MESSAGES

- Switch from TDF to TAF-based regimens is effective in pts on VS
- There is a renal benefit from this switch even in deteriorated pts with eGFR 30-69 mL/min
- TAF and ABC are «lipid neutral»
- After switching from TDF to TAF a small but statistically significant improvement in eGFR was observed
- Elderly pts can derive a real increase in BMD by DXA from switching from TDF to TAF
- Women have a beneficial effect in renal and bone health from this switch