National HIV Curriculum

Elvitegravir-Cobicistat-Tenofovir alafenamide-Emtricitabine (*Genvoya*)

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Elvitegravir-Cobicistat-Tenofovir Alafenamide-Emtricitabine

Elvitegravir-Cobicistat-Tenofovir alafenamide-Emtricitabine

150 mg	150 mg	10 mg	200 mg
INSTI	Booster	NRTI	NRTI

Dose: 1 tablet once daily with food

Elvitegravir-Cobicistat-Tenofovir alafenamide-Emtricitabine

- ***Genvoya* Components**
  - Elvitegravir 150 mg
  - Cobicistat 150 mg
  - Tenofovir alafenamide 10 mg
  - Emtricitabine 200 mg
- **Dosing**: 1 pill daily with food
- **With Renal Impairment:** Do not initiate if CrCl <30 mL/min
- **Pregnancy**: insufficient data
- **Common Adverse Events (≥5%):** Nausea (10%), diarrhea (7%), headache (6%), and fatigue (5%)

Source: Elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine. Prescribing Information.

Elvitegravir-Cobicistat-Tenofovir alafenamide-Emtricitabine Summary of Key Phase 3 Studies

- **Trials in Treatment-Naïve Adults**
  - Study 104 and Study111: EVG-COBI-TAF-FTC vs. EVG-COBI-TDF-FTC
- **Switch Trials in Special Populations**
  - STUDY 112: EVG-COBI-TAF-FTC in Renal Impairment
  - STUDY 1249: EVG-COBI-TAF-FTC in Hepatitis B Coinfection
- **Switch/Simplification Studies**
  - STUDY 109: Switch from TDF-Based Regimens to TAF-Based Regimen
  - STUDY 119: Simplification to EVG-COBI-TAF-FTC Plus DRV

Abbreviations: EVG-COBI-TAF-FTC = elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine; EVG-COBI-TDF-FTC = elvitegravir-cobicistat-tenofovir DF-emtricitabine; TDF = tenofovir DF; TAF = tenofovir alafenamide; DRV = darunavir

Elvitegravir-Cobicistat-Tenofovir Alafenamide-Emtricitabine

Trials in Treatment-Naïve Adults

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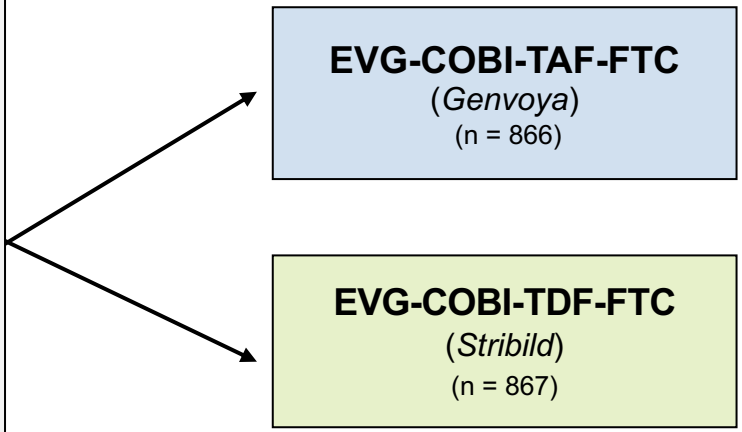
EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC

Study 104 and Study 111

EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC Study 104/111: Design

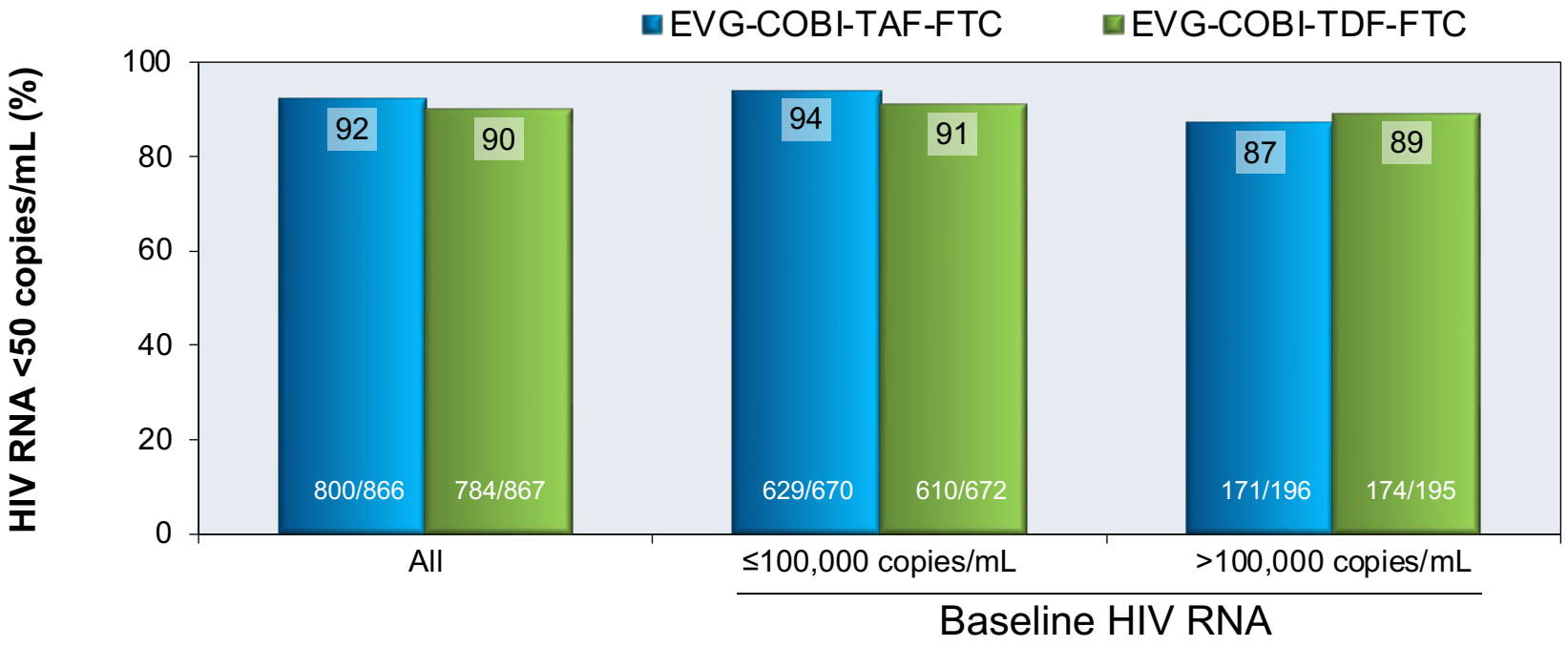
- **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine with elvitegravir-cobicistat-tenofovir DF-emtricitabine
- **Inclusion Criteria** (n = 1,733)
  - Antiretroviral-naïve patients
  - Age >18
  - HIV RNA ≥1000 copies/mL
  - Any CD4 count allowed
  - No AIDS conditions in prior 30 days
- **Treatment Arms**
  - Elvitegravir-Cobicistat-TAF-FTC
  - Elvitegravir-Cobicistat-TDF-FTC



Source: Sax PE, et al. Lancet. 2015;385:2606-15.

EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
Study 104/111: Result

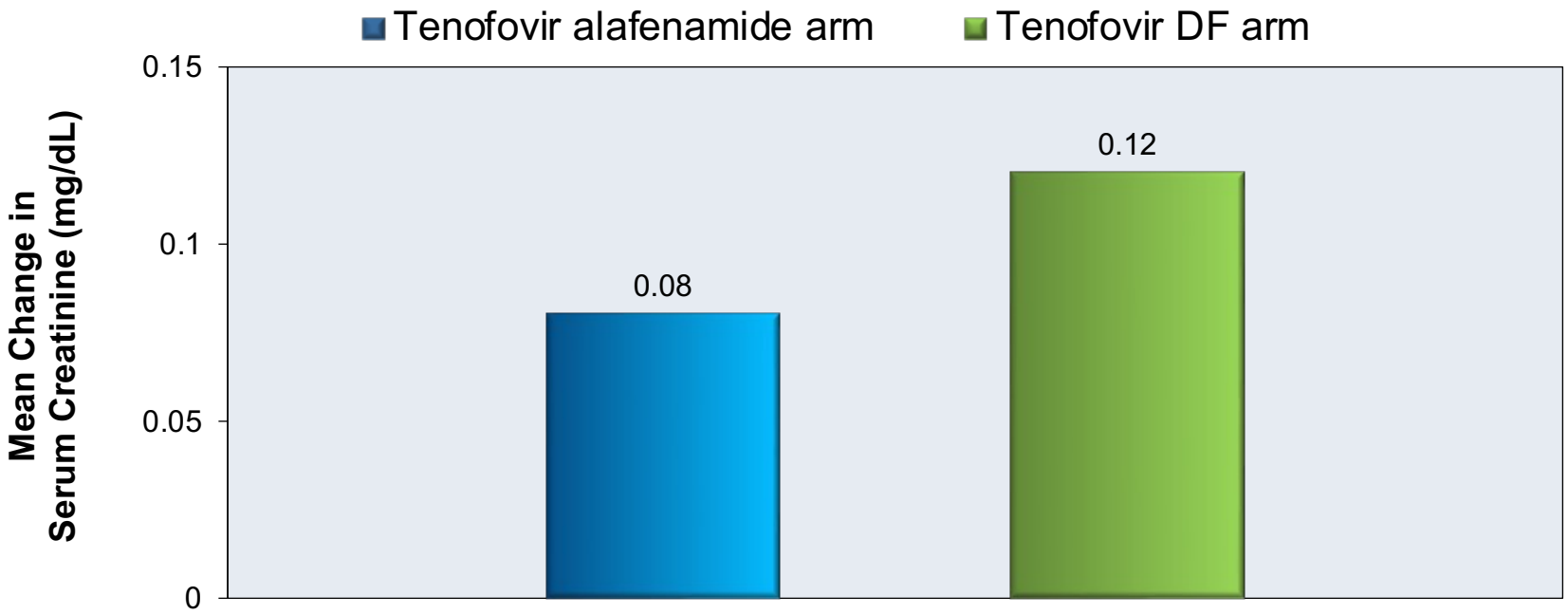
Week 48 Virologic Response (Intent-to-Treat Analysis)



Source: Sax PE, et al. Lancet. 2015;385:2606-15.

EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
Study 104/111: Adverse Effects

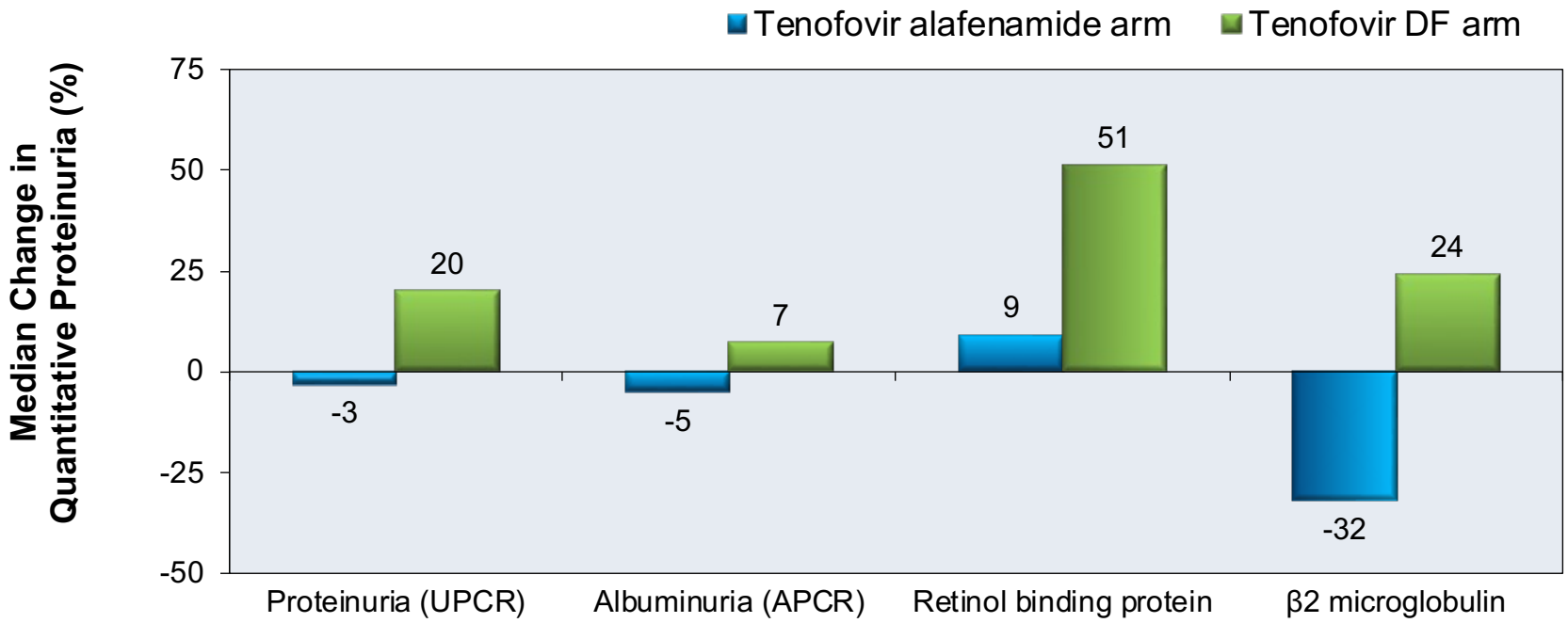
Week 48: Change in Serum Creatinine from Baseline



Source: Sax PE, et al. Lancet. 2015;385:2606-15.

EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
Study 104/111: Adverse Effects

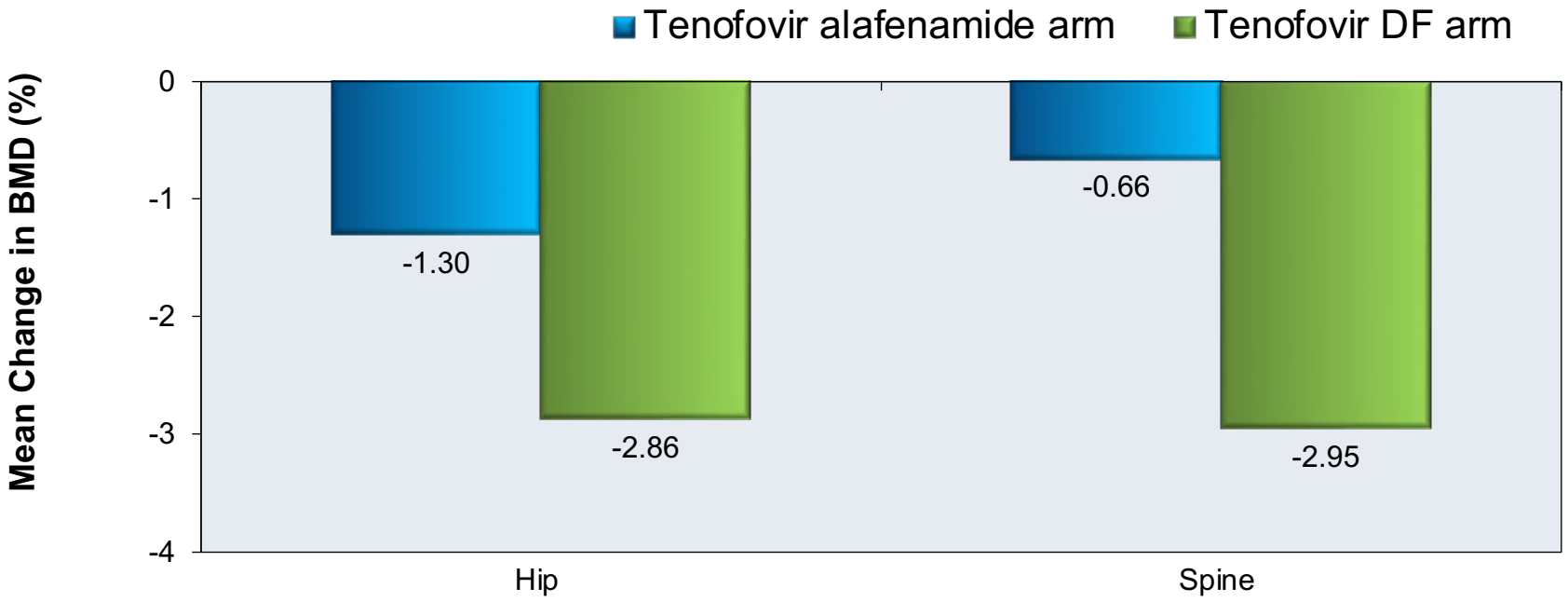
Week 48: Changes in Quantitative Proteinuria from Baseline



Source: Sax PE, et al. Lancet. 2015;385:2606-15.

EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
Study 104/111: Adverse Effects

Week 48: Changes in Spine and Hip Bone Mineral Density (BMD)



Source: Sax PE, et al. Lancet. 2015;385:2606-15.

EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
Study 104/111: Adverse Effects

Week 48: Changes in Lipid Parameters

Median Change from Baseline to Week 48	EVG/COBI/TAF/FTC (n = 866)	EVG/COBI/TDF/FTC (n = 867)	P Value
Total cholesterol	+29	+14	<0.001
LDL	+14	+5	<0.001
HDL	+8	+4	<0.001
Triglycerides	+19	+8	0.027
Total cholesterol:HDL ratio	+0.1	+0.1	0.84

Source: Sax PE, et al. Lancet. 2015;385:2606-15.

EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
Study 104/111: Conclusions

Interpretation: “Through 48 weeks, more than 90% of patients given E/C/F/tenofovir alafenamide or E/C/F/tenofovir disoproxil fumarate had virological success. Renal and bone effects were significantly reduced in patients given E/C/F/tenofovir alafenamide. Although these studies do not have the power to assess clinical safety events such as renal failure and fractures, our data suggest that E/C/F/tenofovir alafenamide will have a favourable long-term renal and bone safety profile.”

Source: Sax PE, et al. Lancet. 2015;385:2606-15.

Elvitegravir-Cobicistat-Tenofovir Alafenamide-Emtricitabine

Switch Studies in Special Populations

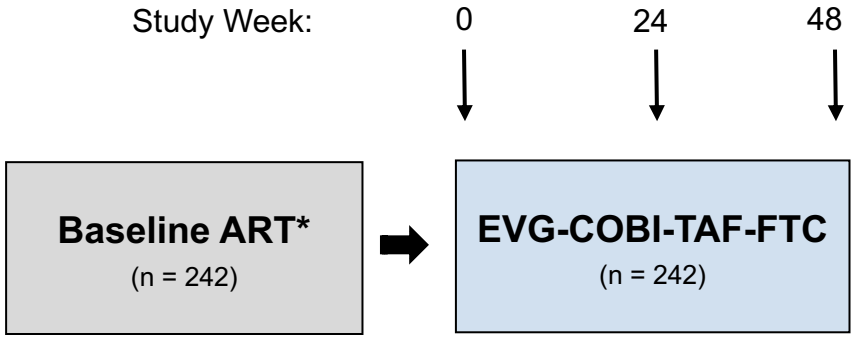
National HIV Curriculum

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment

Study 112

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment
Study 112: Design

- **Background**: Open-label, single-arm, phase 3 trial evaluating switching to once-daily elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine from baseline ART*
- **Inclusion Criteria** (n = 242)
  - HIV RNA < 50 copies/mL for ≥6 months
  - eGFR stable at 30-69 mL/min ≥3 months
  - CD4 ≥50 cells/mm3
  - No new AIDS conditions in past 30 days
  - No resistance to EVG, FTC, or TDF
- **Treatment Arms**
  - Switch to EVG-COBI-TAF-FTC



***Baseline ART**

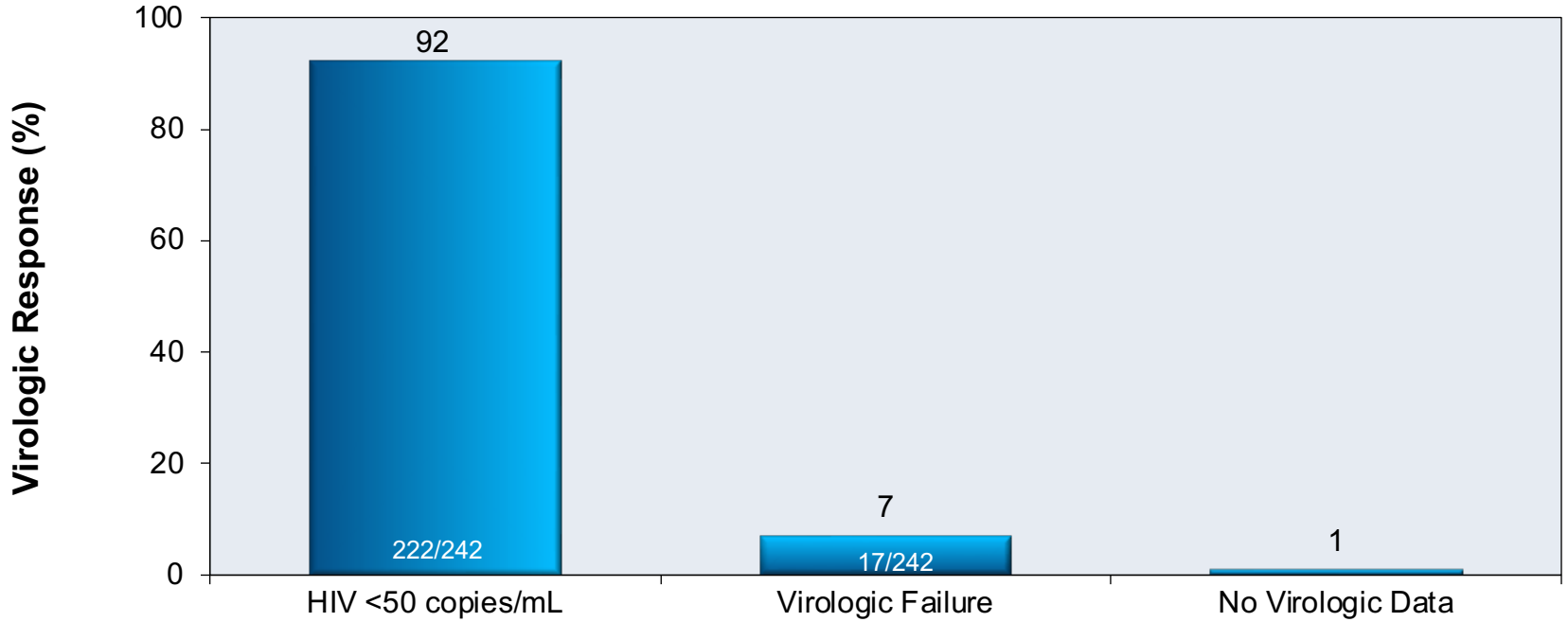
NRTIs: Tenofovir DF 65%, Abacavir 22%, Other NRTI 7%, No NRTI 5%

Third Agent: PI 44%, NNRTI 42%, INSTI 24%, CCR5 Antagonist 3%

Source: Pozniak A, et al. J Acquir Immune Defic Syndr. 2016;71:530-7.

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment Study 112: Result

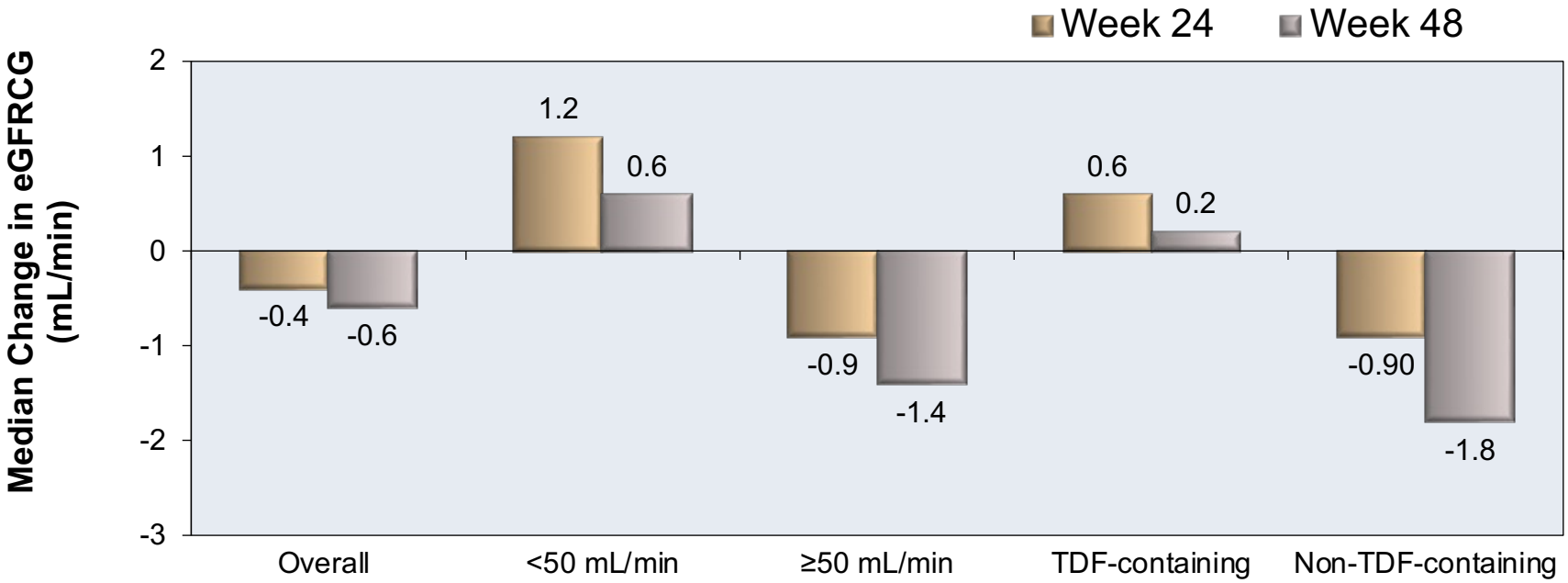
Week 48 Virologic Response



Source: Pozniak A, et al. J Acquir Immune Defic Syndr. 2016;71:530-7.

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment Study 112: Subgroup Analysis Result

Change in Estimated GFR* from Baseline to Weeks 24 and 48

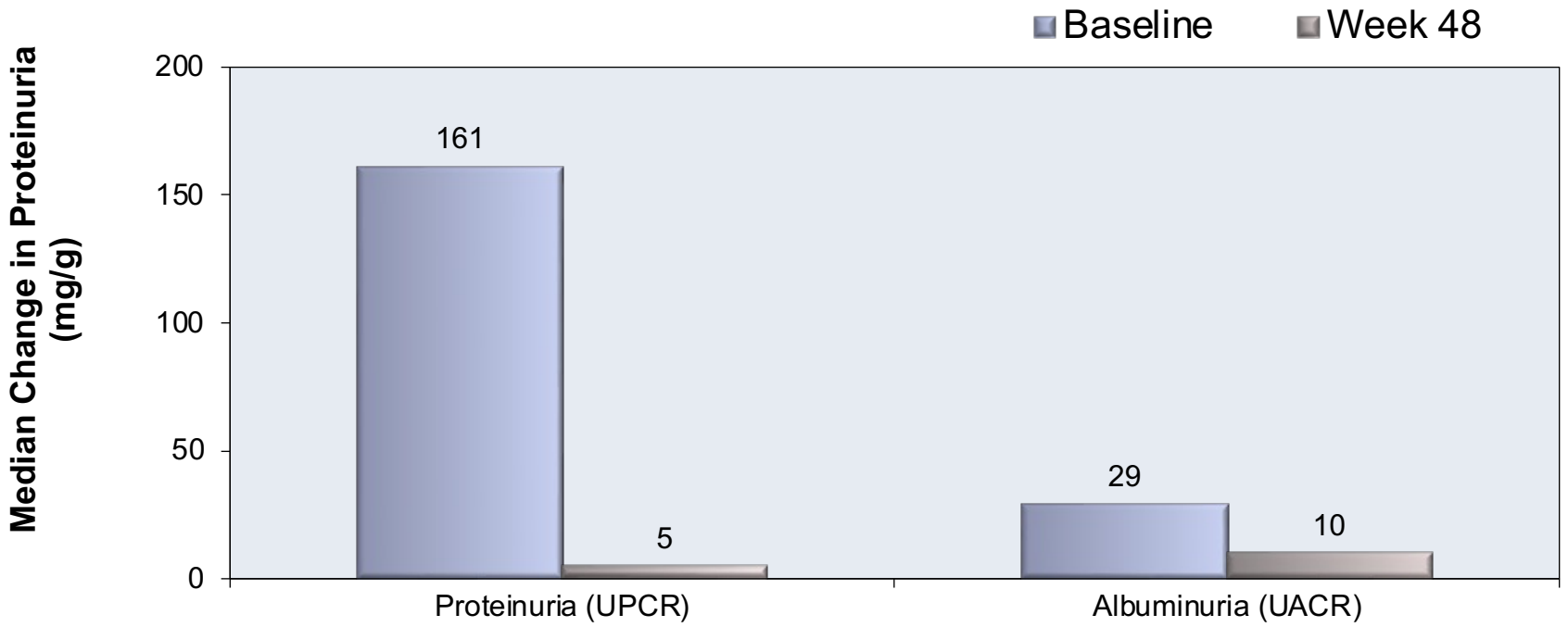


*GFR estimated by Cockcroft Gault

Source: Pozniak A, et al. J Acquir Immune Defic Syndr. 2016;71:530-7.

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment
Study 112: Result

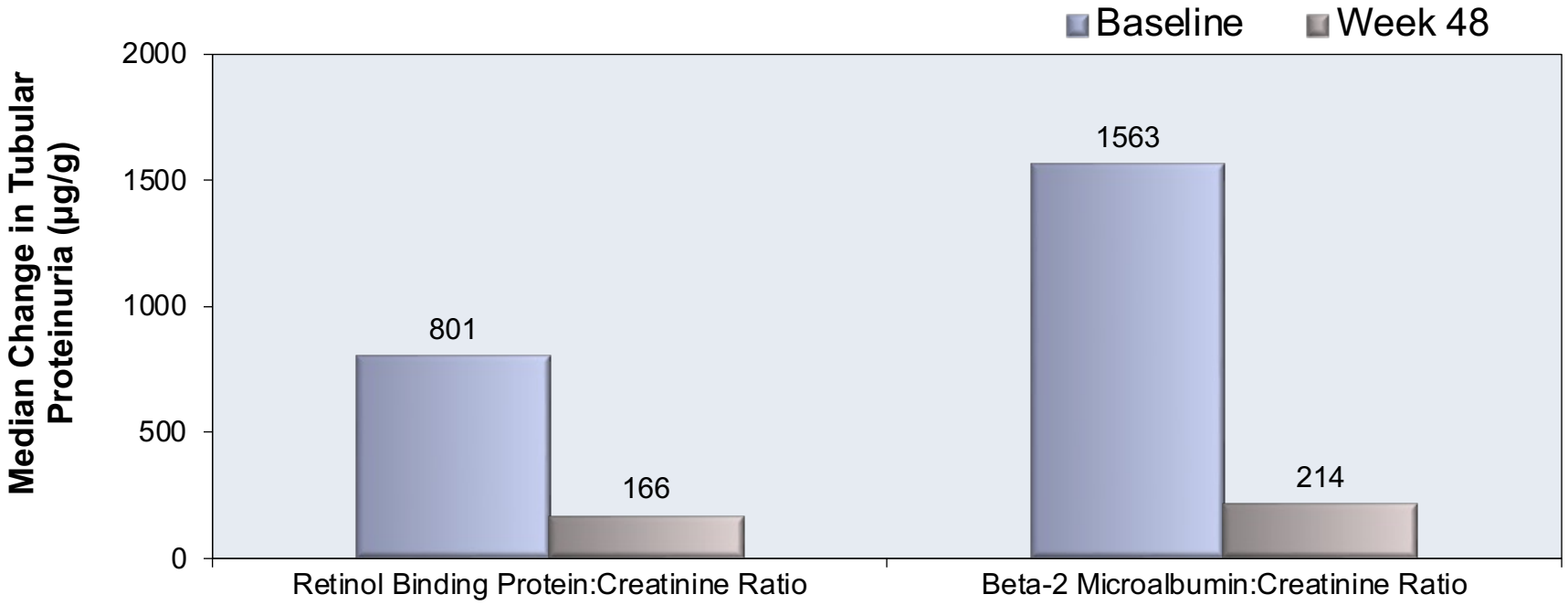
Week 48: Changes in General Proteinuria



Source: Pozniak A, et al. J Acquir Immune Defic Syndr. 2016;71:530-7.

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment
Study 112: Result

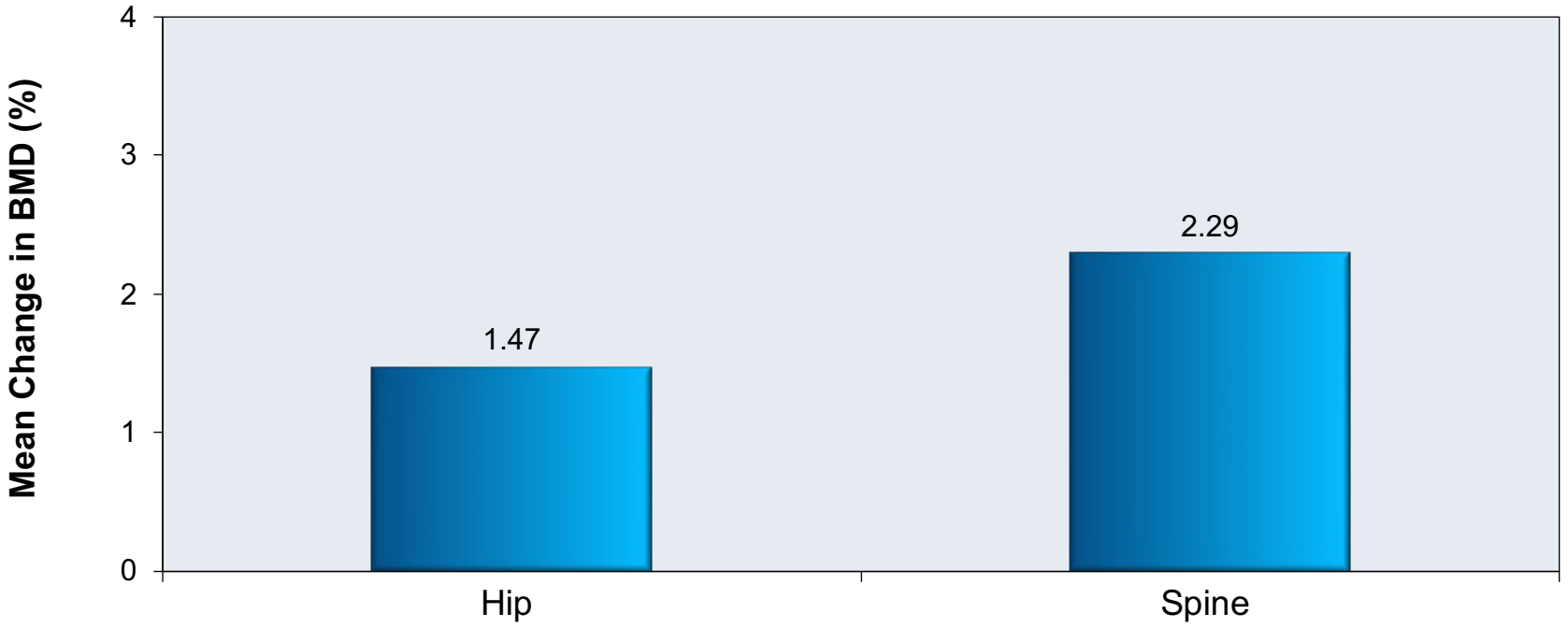
Week 48: Changes in Tubular Proteinuria



Source: Pozniak A, et al. J Acquir Immune Defic Syndr. 2016;71:530-7.

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment
Study 112: Result

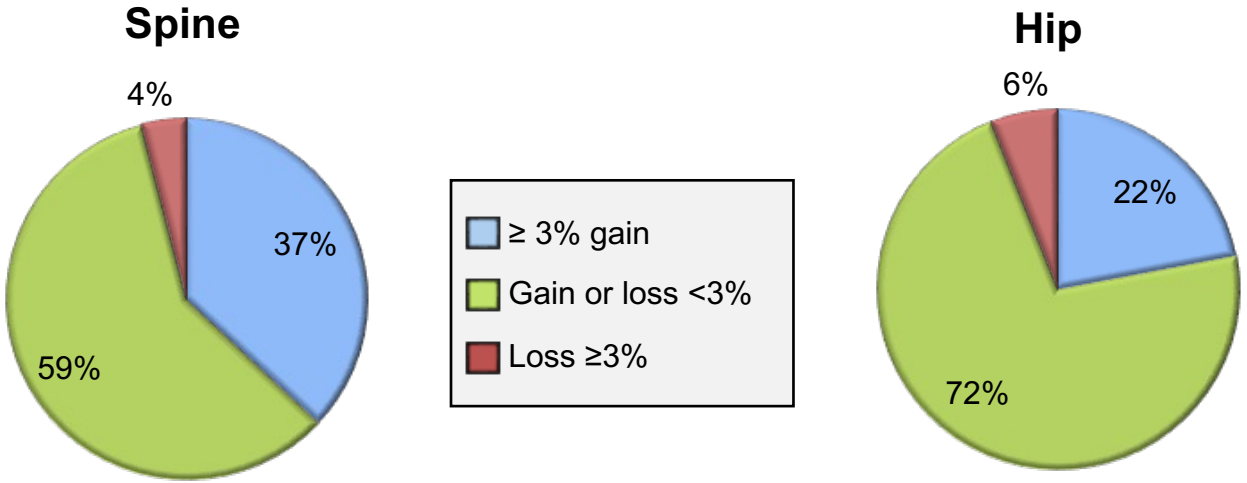
Week 48: Changes in Bone Mineral Density (BMD)



Source: Pozniak A, et al. J Acquir Immune Defic Syndr. 2016;71:530-7.

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment Study 112: Result

Week 48: Changes in Spine and Hip Bone Mineral Density (BMD)



Source: Pozniak A, et al. J Acquir Immune Defic Syndr. 2016;71:530-7.

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment
Study 112: Conclusions

Interpretation: “Switch to E/C/F/TAF was associated with minimal change in GFR. Proteinuria, albuminuria and bone mineral density significantly improved. These data support the efficacy and safety of once daily E/C/F/TAF in HIV+ patients with mild or moderate renal impairment without dose adjustment.”

Source: Gallant J, et al. J Acquir Immune Defic Syndr. 2016;73:294-8.

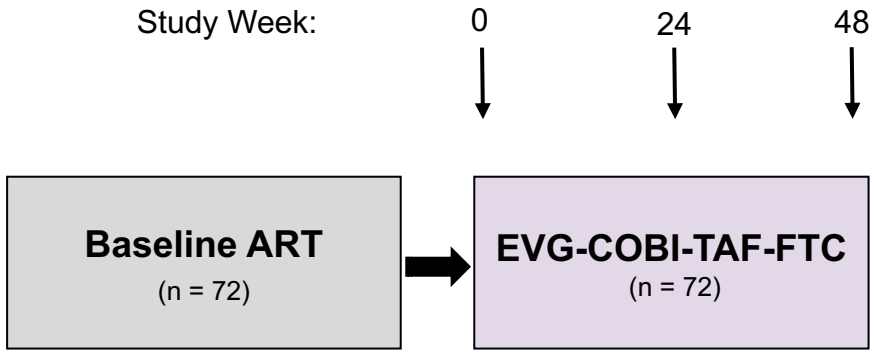
Elvitegravir-Cobicistat-TAF-FTC in Hepatitis B Coinfection

Study 1249

National HIV Curriculum

Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection Study 1249: Design

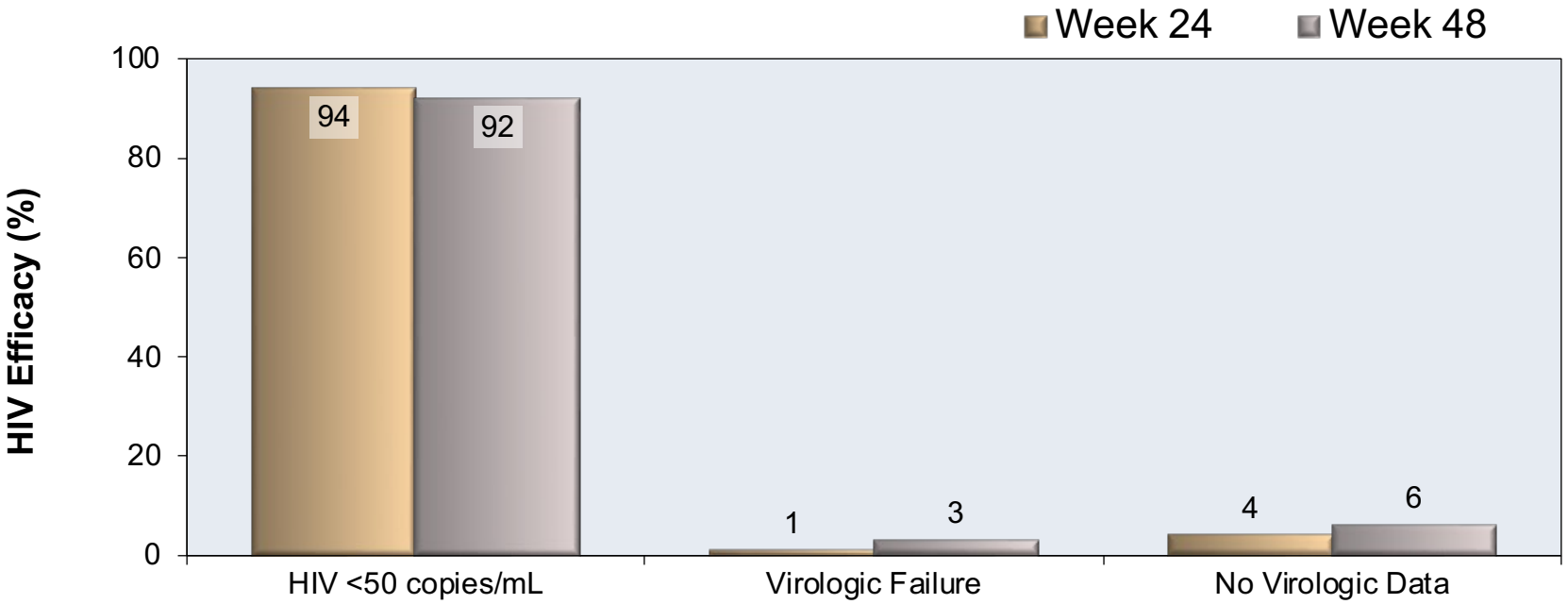
- **Background**: Open-label, single-arm, phase 3b trial evaluating switching to once-daily elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine in adults with HIV and HBV
- **Inclusion Criteria** (n = 72)
  - Adults with HIV and chronic HBV
  - HIV RNA <50 copies/mL for ≥6 months
  - Stable ART regimen for ≥4 months
  - CD4 ≥200 cells/mm^3
  - CrCl ≥50 mL/min, ALT ≤10x ULN
  - No cirrhosis, HCC, HCV, hepatitis D
- **Treatment Arms**
  - Switch to EVG-COBI-TAF-FTC



Source: Gallant J, et al. J Acquir Immune Defic Syndr. 2016;73:294-8.

Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection Study 1249: Result

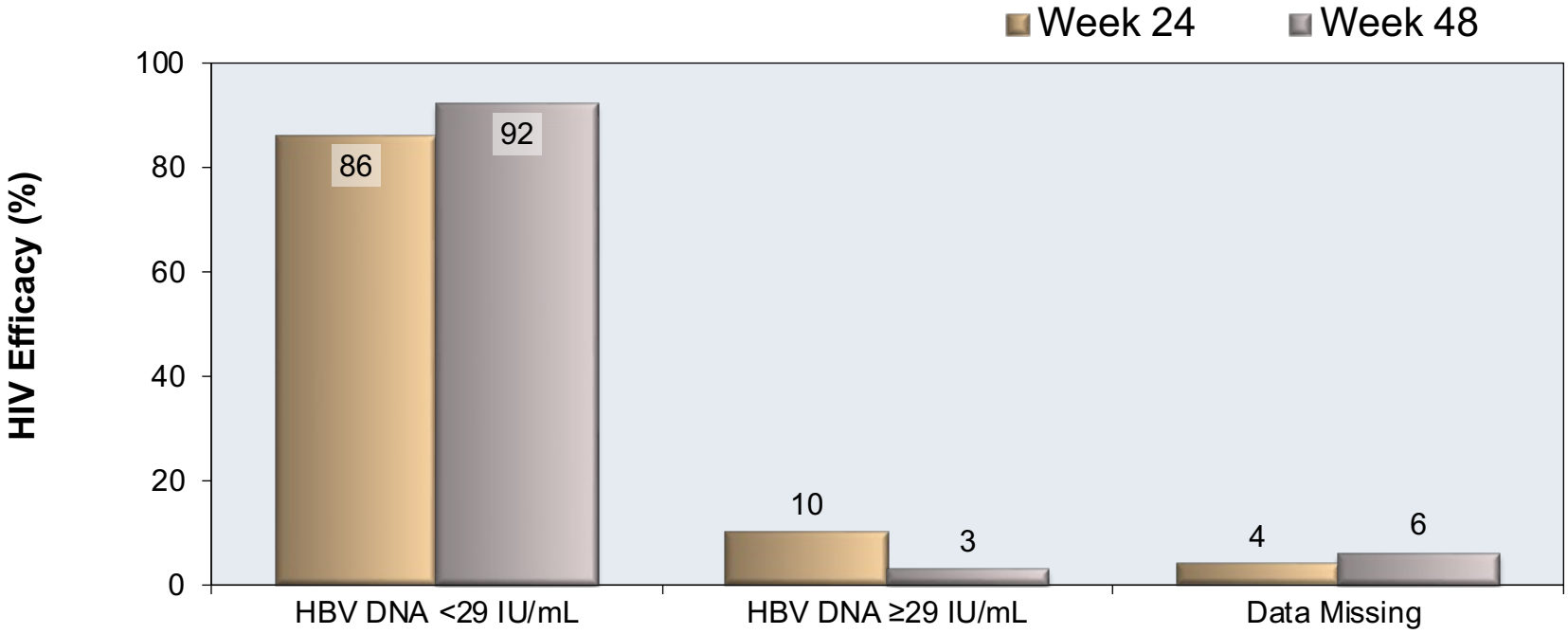
HIV Efficacy at Weeks 24 and 48



Source: Gallant J, et al. J Acquir Immune Defic Syndr. 2016;73:294-8.

Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection Study 1249: Result

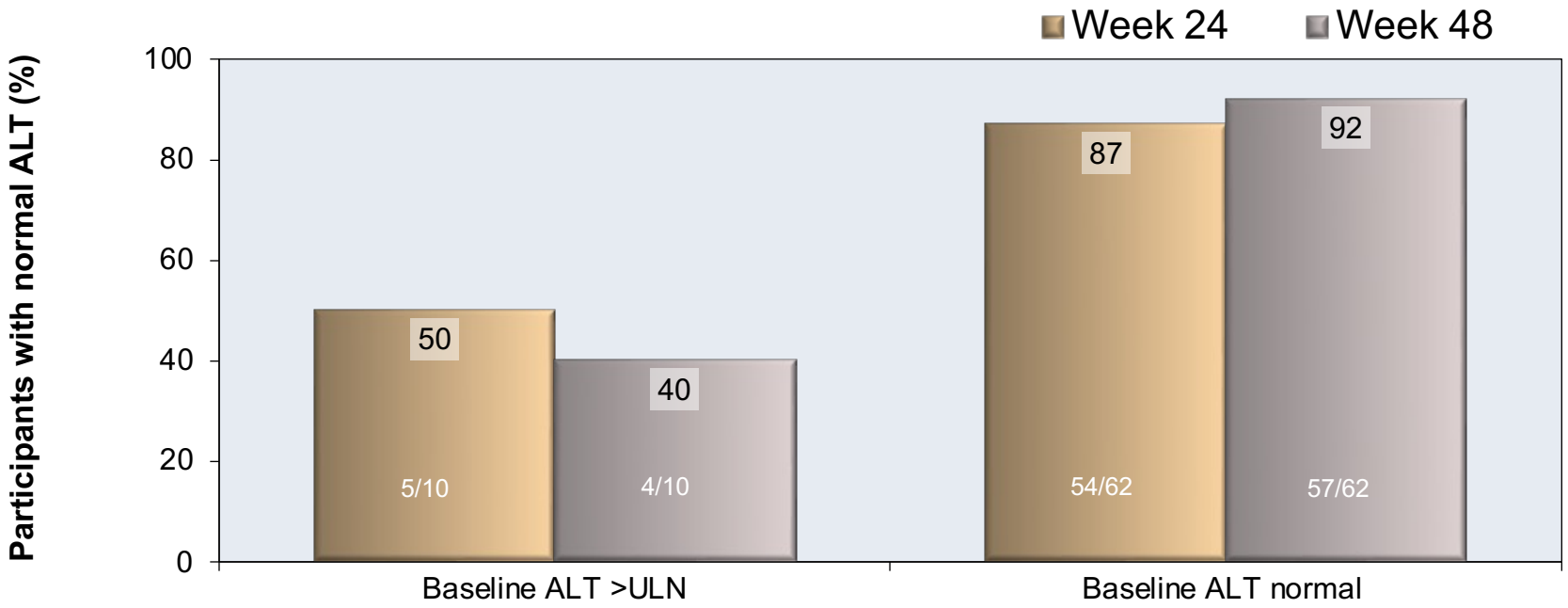
HBV Efficacy at Weeks 24 and 48, Missing = Failure



Source: Gallant J, et al. J Acquir Immune Defic Syndr. 2016;73:294-8.

Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection Study 1249: Subgroup Analysis Result

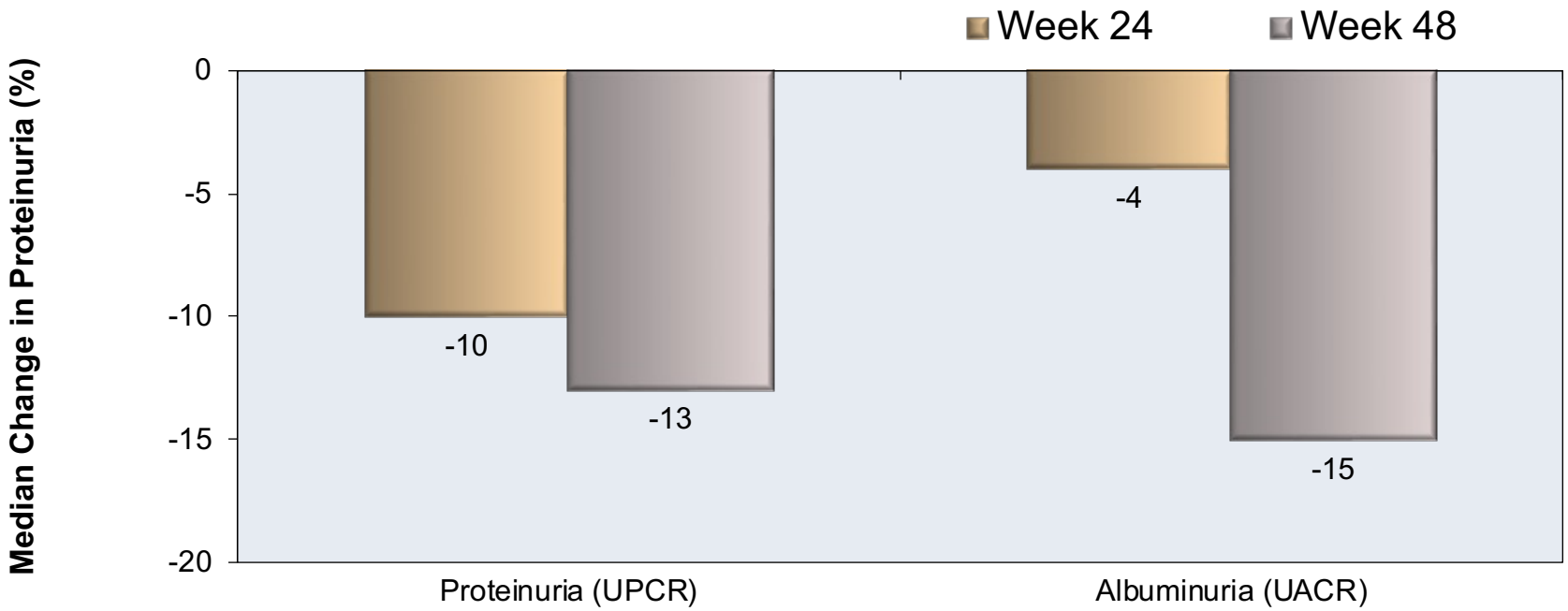
ALT Measurement at Weeks 24 and 48



Source: Gallant J, et al. J Acquir Immune Defic Syndr. 2016;73:294-8.

Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection Study 1249: Result

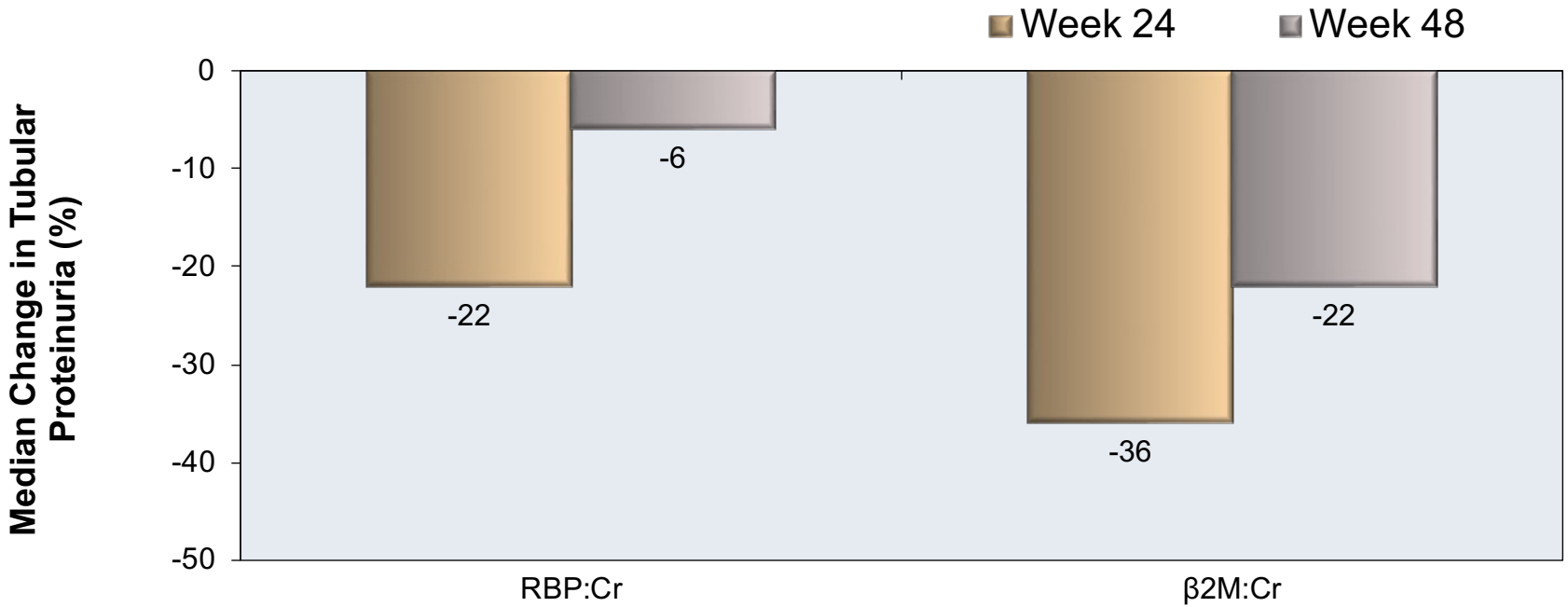
Changes in General Proteinuria at Weeks 24 and 48 from Baseline



Source: Gallant J, et al. J Acquir Immune Defic Syndr. 2016;73:294-8.

Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection Study 1249: Result

Changes in Tubular Proteinuria at Weeks 24 and 48 from Baseline



RBP:Cr = retinol binding protein:creatinine ratio; β2M:Cr = beta-2 microalbumin:creatinine ratio

Source: Gallant J, et al. J Acquir Immune Defic Syndr. 2016;73:294-8.

Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection Study 1249: Conclusions

Interpretation: “In this first study in HIV/HBV-coinfected participants with suppressed HIV infection, E/C/F/TAF was effective against HIV and HBV, well tolerated, and demonstrated improvements in renal and bone safety consistent with the clinical profile of TAF. These data support the use of E/C/F/TAF in treating HIV/HBV coinfections.”

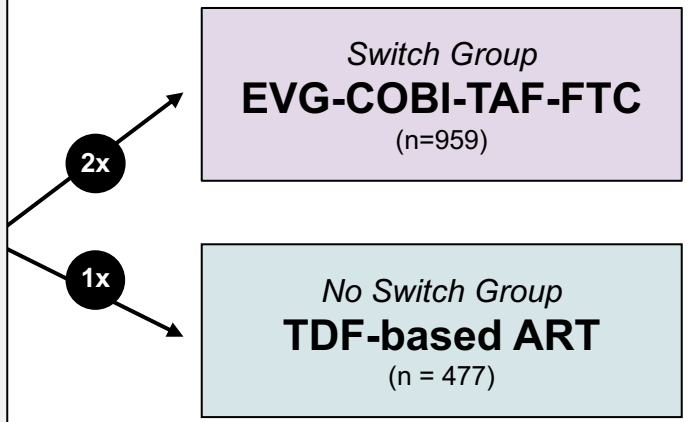
Source: Gallant J, et al. J Acquir Immune Defic Syndr. 2016;73:294-8.

Switch from TDF-based ART to Elvitegravir-Cobicistat-TAF-FTC

Study 109

Switch to Elvitegravir-Cobicistat-TAF-FTC
Study 109: Design

- **Background**: Open-label, randomized, phase 3 trial comparing switch to EVG-COBI-TAF-FTC versus continuation of baseline regimen of TDF-based ART
- **Inclusion Criteria** (n = 1443)
  - HIV RNA < 50 copies/mL on ART for ≥96 weeks
  - CrCl >50 mL/min
  - 1 of 4 baseline TDF-containing ART regimens:
    - EVG-COBI-TDF-FTC (n=459)
    - EFV-TDF-FTC (n=376)
    - ATV + RTV + TDF-FTC (n=385)
    - ATV-COBI + TDF-FTC (n=216)
- **Treatment Arms**
  - EVG-COBI-TAF-FTC (Switch group)
  - Remain on TDF-based ART (No switch group)

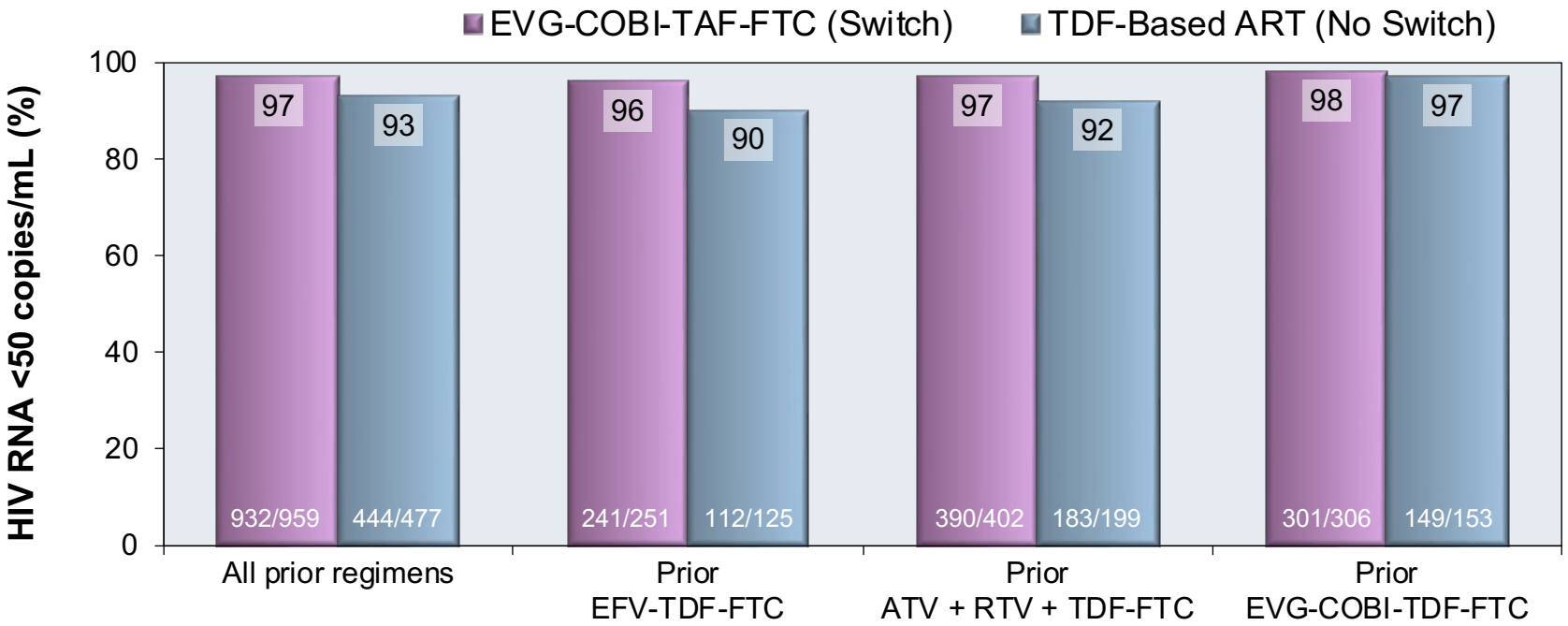


*__NOTE__: Between randomization and study onset, 4 participants withdrew consent, 2 withdrew by investigator discretion, and 1 was lost to follow-up.

Source: Mills A, et al. Lancet Infect Dis. 2016;16:43-52.

Switch to Elvitegravir-Cobicistat-TAF-FTC
Study 109: Subgroup Analysis Result

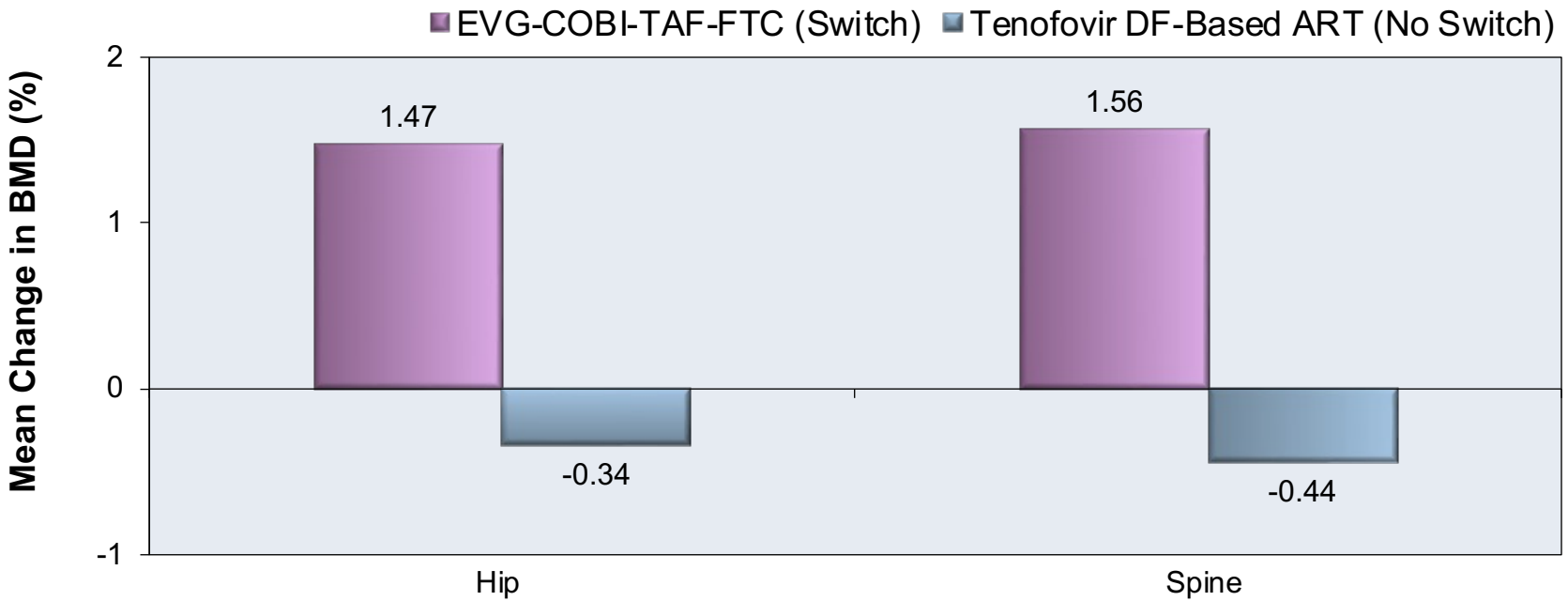
Week 48 Virologic Response, by Baseline Regimen



Source: Mills A, et al. Lancet Infect Dis. 2016;16:43-52.

Switch to Elvitegravir-Cobicistat-TAF-FTC
Study 109: Result

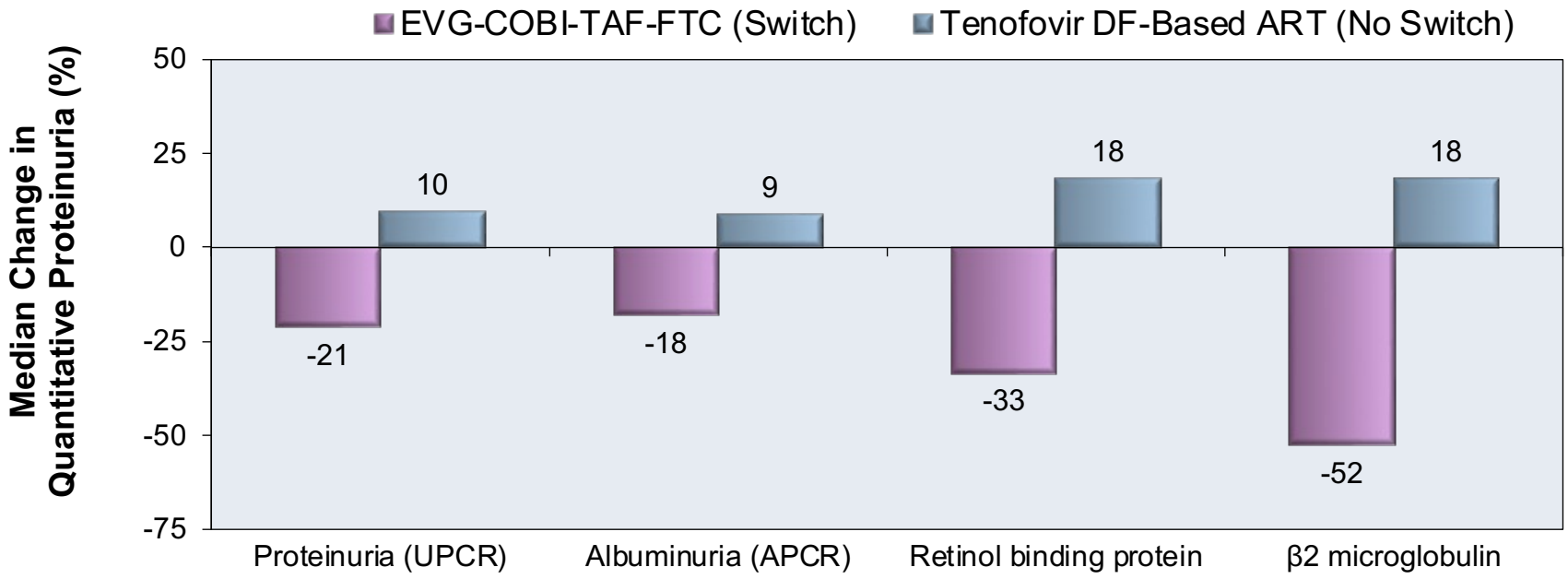
Week 48: Changes in Bone Mineral Density (BMD)



Source: Mills A, et al. Lancet Infect Dis. 2016;16:43-52.

Switch to Elvitegravir-Cobicistat-TAF-FTC
Study 109: Result

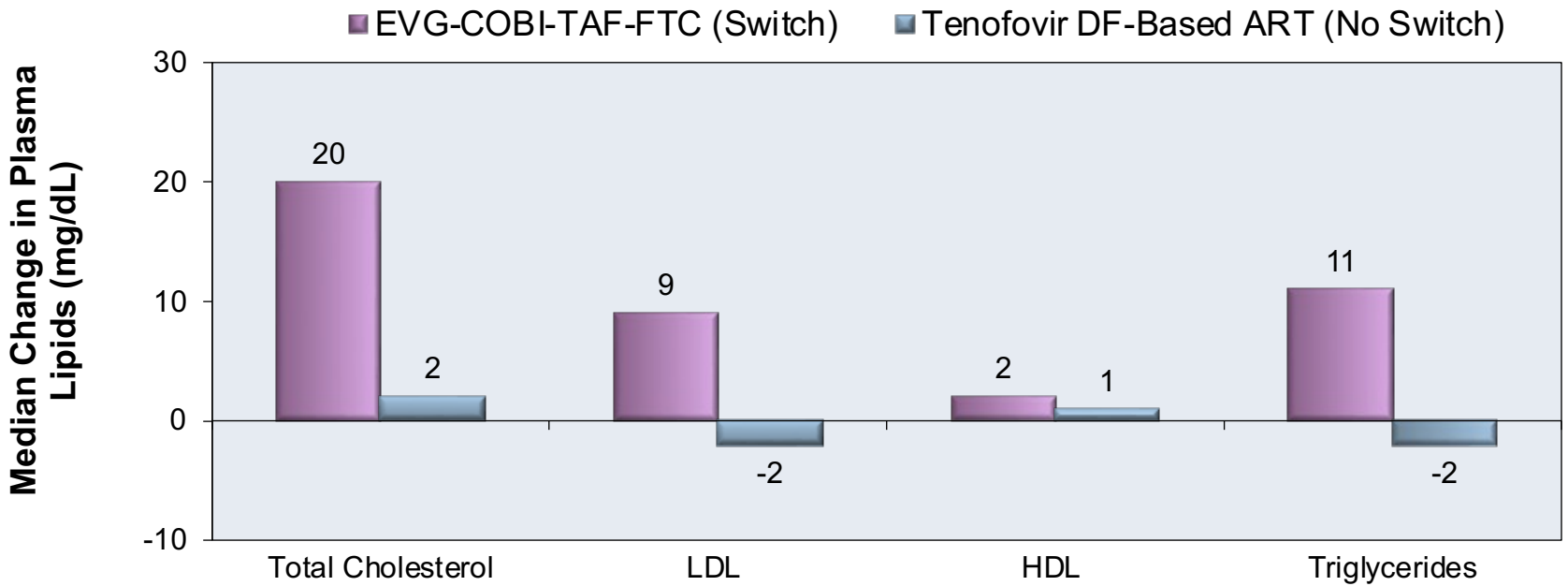
Week 48: Changes in Quantitative Proteinuria from Baseline



Source: Mills A, et al. Lancet Infect Dis. 2016;16:43-52.

Switch to Elvitegravir-Cobicistat-TAF-FTC
Study 109: Result

Week 48: Change in Plasma Lipids from Baseline



Source: Mills A, et al. Lancet Infect Dis. 2016;16:43-52.

Switch to Elvitegravir-Cobicistat-TAF-FTC
Study 109: Conclusions

Interpretation: “Switching to a tenofovir alafenamide-containing regimen from one containing tenofovir disoproxil fumarate was non-inferior for maintenance of viral suppression and led to improved bone mineral density and renal function. Longer term follow-up is needed to better understand the clinical impact of these changes.”

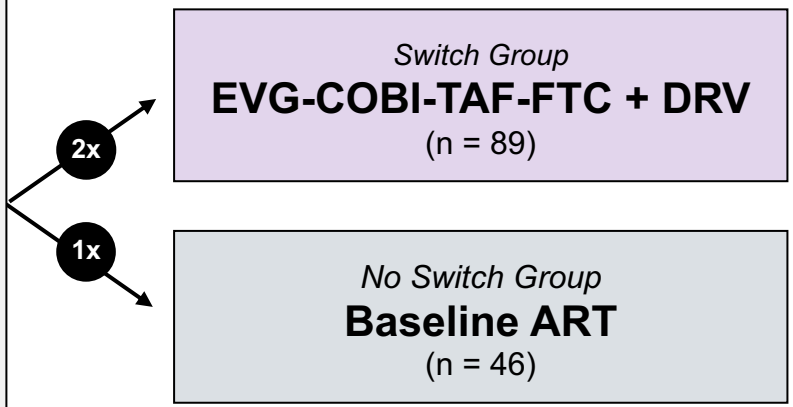
Source: Mills A, et al. Lancet Infect Dis. 2016;16:43-52.

Simplification to EVG-COBI-TAF-FTC plus Darunavir

Study 119

Simplification to EVG-COBI-TAF-FTC plus DRV Study 119: Design

- **Background**: Open-label, randomized, phase 3 trial comparing simplification to EVG-COBI-TAF-FTC plus darunavir versus continuation of baseline salvage ART regimen containing darunavir
- **Inclusion Criteria** (n = 135)
  - HIV RNA <50 copies/mL on DRV-containing regimen
  - On regimen for ≥4 months
  - At least 2 prior regimen failures and ≥2-class DRMs
  - No DRV RAMs, no INSTI resistance, ≤3 TAMs, no Q151M or T69 insertion
- **Treatment Arms**
  - EVG-COBI-TAF-FTC + DRV (Switch group)
  - Remain on baseline ART (No switch group)



*__Abbreviations__: RAM = resistance associated mutation, INSTI = integrase strand transfer inhibitor, TAM's = thymidine analogue mutations

Source: Huhn GD, et al. J Acquir Immune Defic Syndr. 2017;74:193-200.

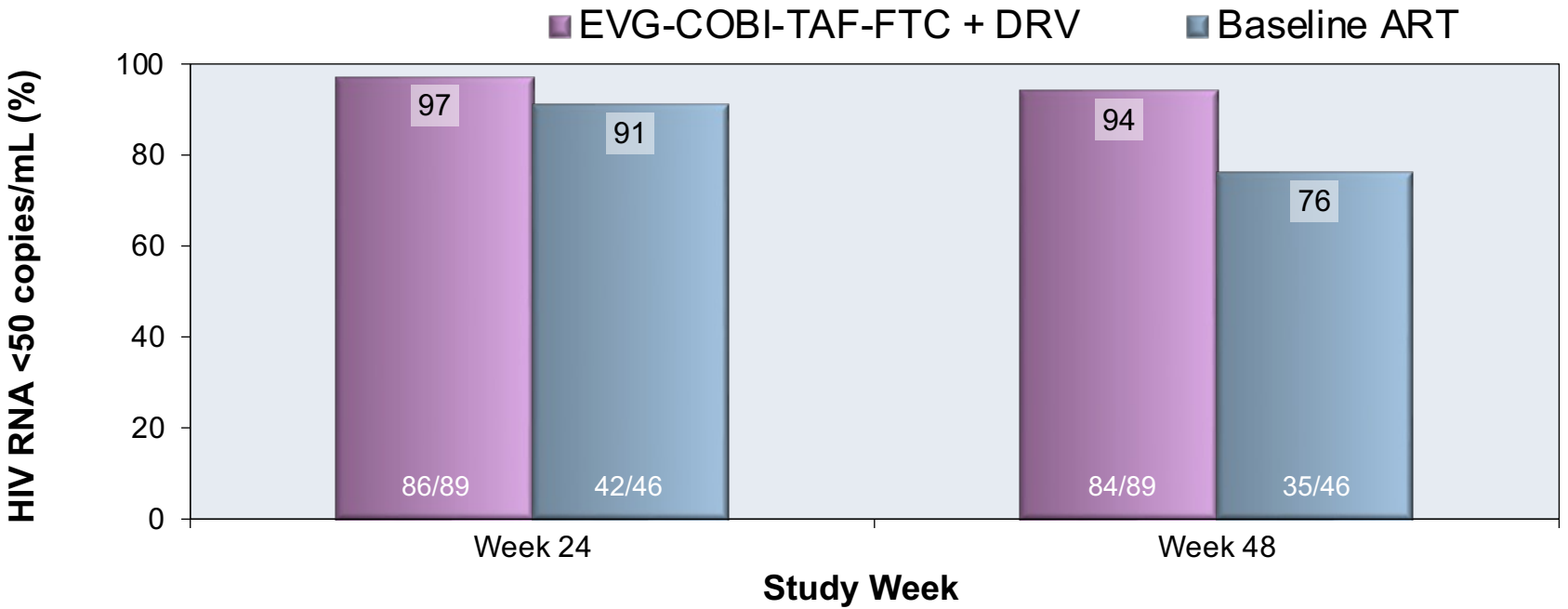
Simplification to EVG-COBI-TAF-FTC plus DRV
Study 119: Design

Characteristics	EVG-COBI-TAF-FTC + DRV (n = 89)	Baseline Regimen (n = 46)
Median age, years	49	47
Male	82	61
Black (or African descent)	39	57
Median CD4 count, cells/mL	519	518
Median eGFR, mL/min (Cockroft-Gault)	99	100
Median # pills per day in ART regimen	5	5
≥6 pills per day in ART regimen, %	40	37
At least BID dosing, %	65	65
Tenofovir, %	61	54
Raltegravir, %	56	50
2 class / 3 class resistance, %	70 / 26	74 / 20
M184V/I / K65R, %	85 / 20	78 / 30
NNRTI resistance / PI resistance	89 / 38	87 / 28

Source: Huhn GD, et al. J Acquir Immune Defic Syndr. 2017;74:193-200.

Simplification to EVG-COBI-TAF-FTC plus DRV
Study 119: Results

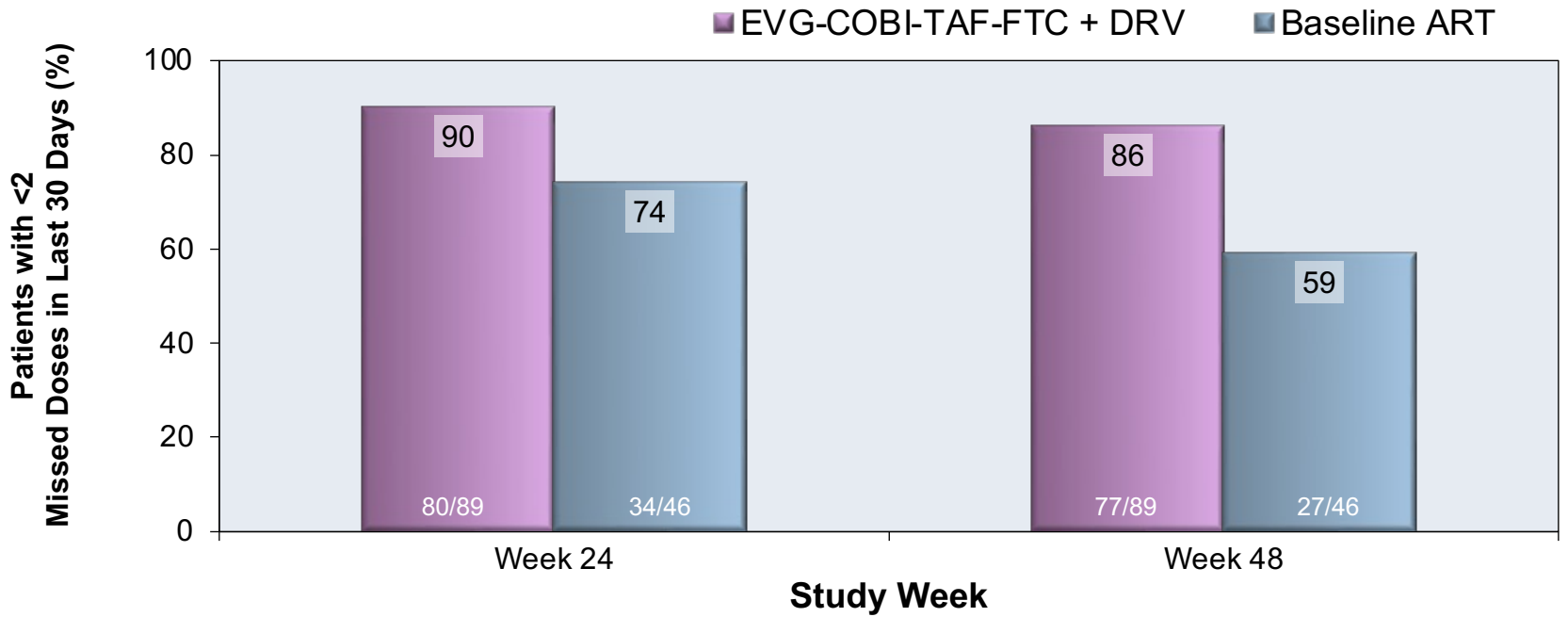
Week 24 and 48: Virologic Response (Full analysis set)



Source: Huhn GD, et al. J Acquir Immune Defic Syndr. 2017;74:193-200.

Simplification to EVG-COBI-TAF-FTC plus DRV
Study 119: Results

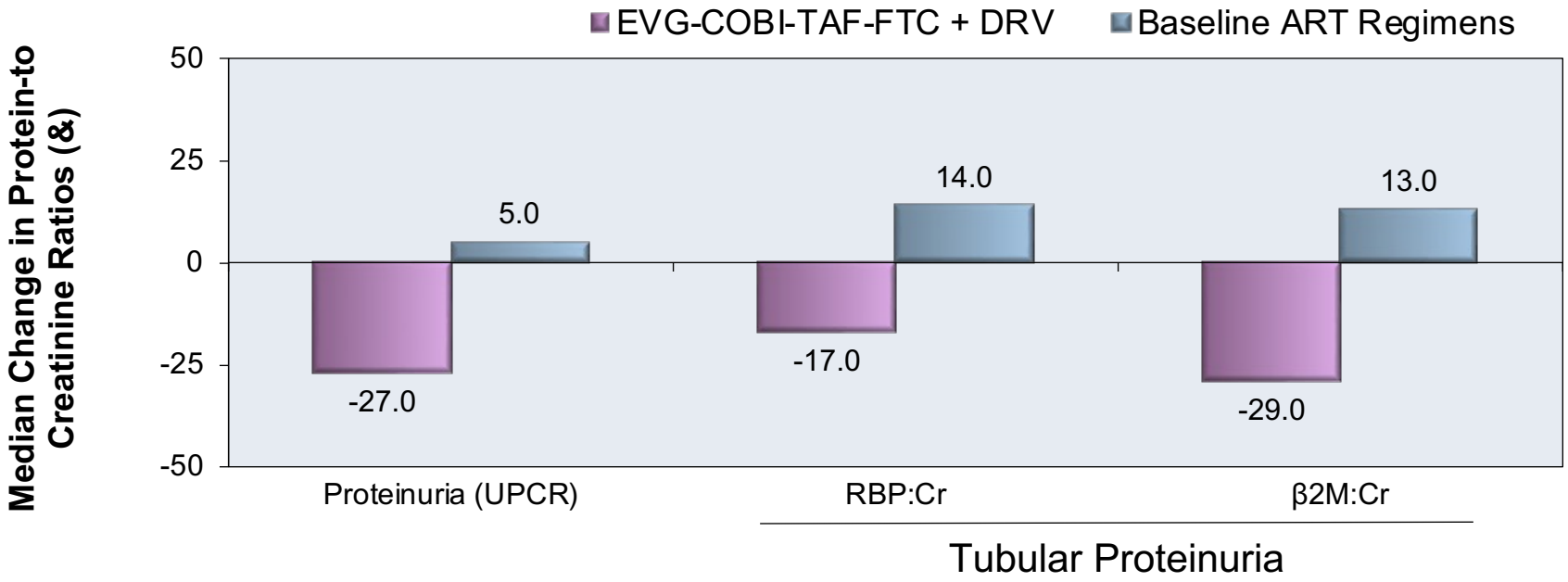
Week 24 and 48: Medication Adherence



Source: Huhn GD, et al. J Acquir Immune Defic Syndr. 2017;74:193-200.

Simplification to EVG-COBI-TAF-FTC plus DRV
Study 119: Result

Week 48: Urine Protein-to-Creatinine Ratios from Baseline



Abbreviations: RBP:Cr = retinol binding protein:creatinine ratio; β2M:Cr = beta-2 microalbumin:creatinine ratio

Source: Huhn GD, et al. J Acquir Immune Defic Syndr. 2017;74:193-200.

Simplification to EVG-COBI-TAF-FTC plus DRV
Study 119: Conclusions

Conclusions: “This study demonstrated that regimen simplification from a 5-tablet regimen to the 2-tablet, once-daily combination of E/C/F/TAF plus DRV has durable maintenance of virologic suppression and improvements in specific markers of renal safety. Such a strategy may lead to greater adherence and improved quality of life.”

Source: Huhn GD, et al. J Acquir Immune Defic Syndr. 2017;74:193-200.

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