National HIV Curriculum

Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine (*Stribild*)

Prepared by:

David H. Spach, MD
Brian R. Wood, MD

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Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

150 mg	150 mg	300 mg	200 mg
INSTI	Booster	NRTI	NRTI

Dose: 1 tablet once daily with food

Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

- ***Stribild* Components**:
  - Elvitegravir 150 mg
  - Cobicistat 150 mg
  - Emtricitabine 200 mg
  - Tenofovir disoproxil fumarate 300 mg
- **Dosing**: 1 pill daily with food (separate ≥ 2 hours with antacids)
- **With Renal Impairment**
  - Do ***not*** initiate if CrCl <70 mL/min
  - Discontinue if CrCl <50 mL/min
- **Pregnancy**: category B
- **Common Adverse Events (≥5%)**
  - Nausea, diarrhea, abnormal dreams, headache, and fatigue

Source: Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine. Prescribing Information.

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

- **Trials in Treatment Naïve**
  - Study 102: EVG-COBI-TDF-FTC vs. EFV-TDF-FTC
  - Study 103: EVG-COBI-TDF-FTC vs. RTV + ATV + TDF-FTC
  - Study 104/111: EVG-COBI-TAF-FTC vs. EVG-COBI-TDF-FTC
  - Study 128 (WAVES): EVG-COBI-TDF-FTC vs. RTV + ATV + TDF-FTC
- **Switch Trials**
  - Study 115 (STRATEGY PI): PI Switch to EVG-COBI-TDF-FTC
  - Study 121 (STRATEGY NNRTI): NNRTI Switch to EVG-COBI-TDF-FTC
  - Study 123: Raltegravir Switch

Abbreviations: EVG-COBI-TDF-FTC = elvitegravir-cobicistat-tenofovir DF-emtricitabine; EFV-TDF-FTC = efavirenz-tenofovir DF-emtricitabine; RTV = ritonavir; ATV = atazanavir; TDF-FTC = tenofovir DF-emtricitabine; EVG-COBI-TAF-FTC = elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine; PI = protease inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor

Initial Therapy

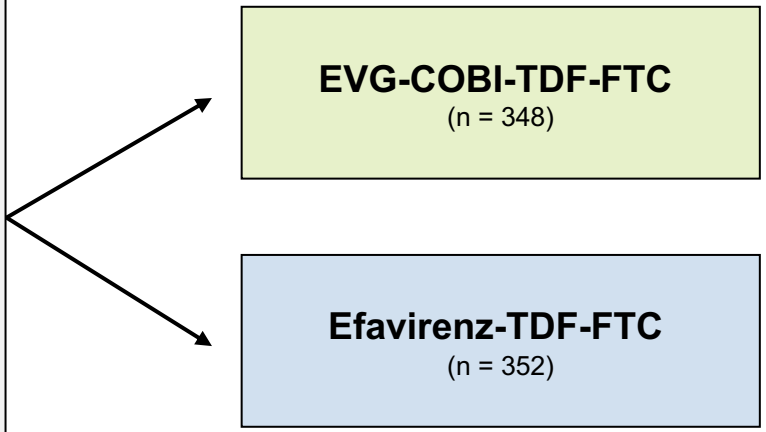
Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC

Study 102

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC Study 102: Design

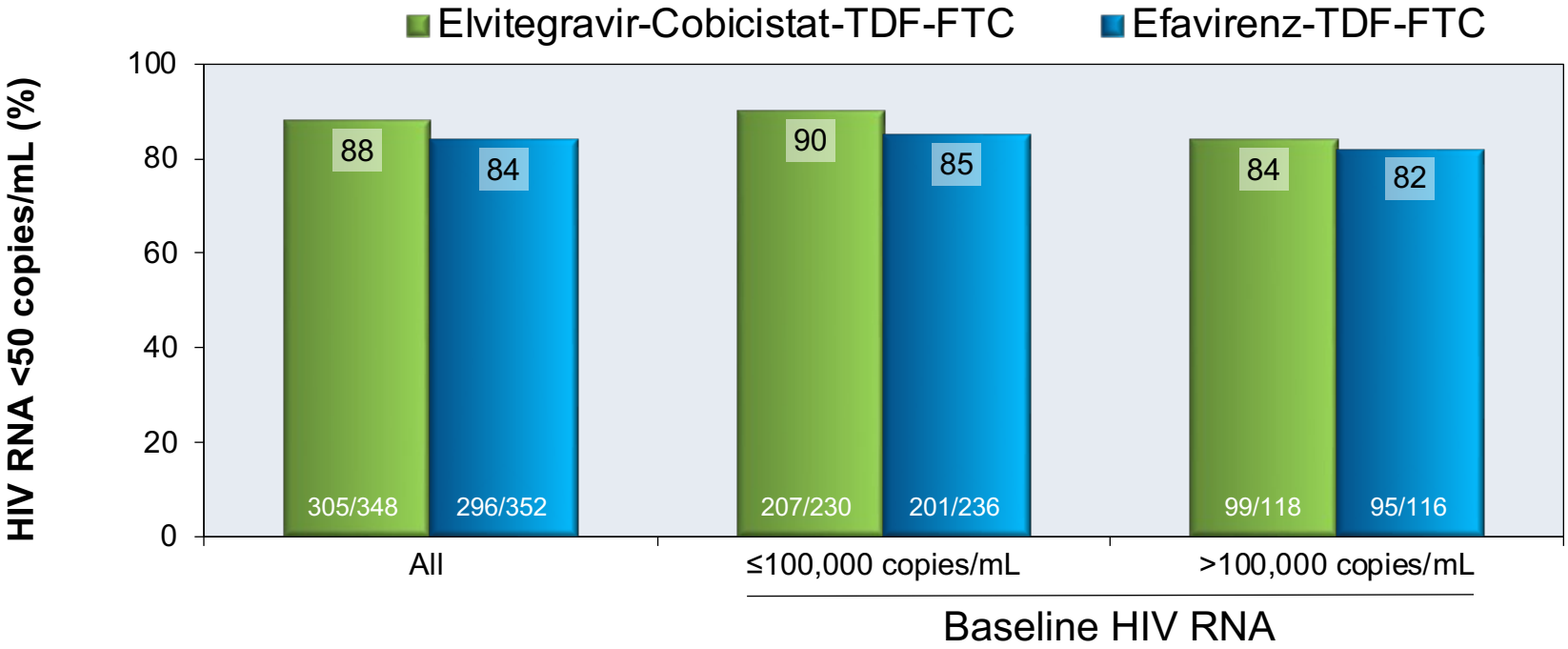
- **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir DF-emtricitabine with efavirenz-tenofovir DF-emtricitabine
- **Inclusion Criteria** (n = 700)
  - Antiretroviral-naïve adults
  - Age ≥18 years
  - HIV RNA ≥5,000 copies/mL
  - No AIDS conditions in previous 30 days
- **Treatment Arms**
  - Elvitegravir-Cobicistat-TDF-FTC
  - Efavirenz-TDF-FTC



Source: Sax PE, et al. Lancet. 2012;379:2439-48.

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC Study 102: Result

Week 48 Virologic Response



Source: Sax PE, et al. Lancet. 2012;379:2439-48.

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC Study 102: Common Adverse Events

Treatment Emergent Adverse Events in ≥ 10% of Subjects in Either Group	EVG-COBI-TDF-FTC (n = 348)	EFV-TDF-FTC (n= 352)
Diarrhea	23%	19%
Nausea*	21%	14%
Fatigue	11%	13%
Upper Respiratory Tract Infection	14%	11%
Dizziness^	7%	24%
Headache	14%	10%
Abnormal Dreams^	15%	27%
Insomnia†	9%	14%
Depression	9%	11%
Rash §	6%	12%

*p < 0.016; ^p < 0.001; †p < 0.031; § p = 0.009

Source: Sax PE, et al. Lancet. 2012;379:2439-48.

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC Study 102: Conclusions

Interpretation: “This study met the primary endpoint of non-inferiority of elvitegravir/cobicistat/emtricitabine/tenofovir (EVG/COBI/TDF/FTC) to efavirenz/emtricitabine/tenofovir (EFV/TDF/FTC) and demonstrates the robust antiviral efficacy of the only integrase inhibitor-based single tablet regimen for initial HIV treatment, irrespective of viral load.”

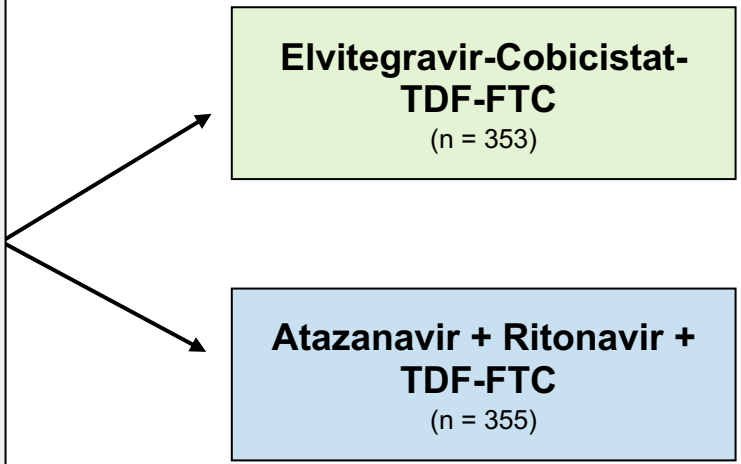
Source: Sax PE, et al. Lancet. 2012;379:2439-48.

EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC

Study 103

Elvitegravir-Cobicistat-TDF-FTC versus Atazanavir + Ritonavir + TDF-FTC Study 103: Design

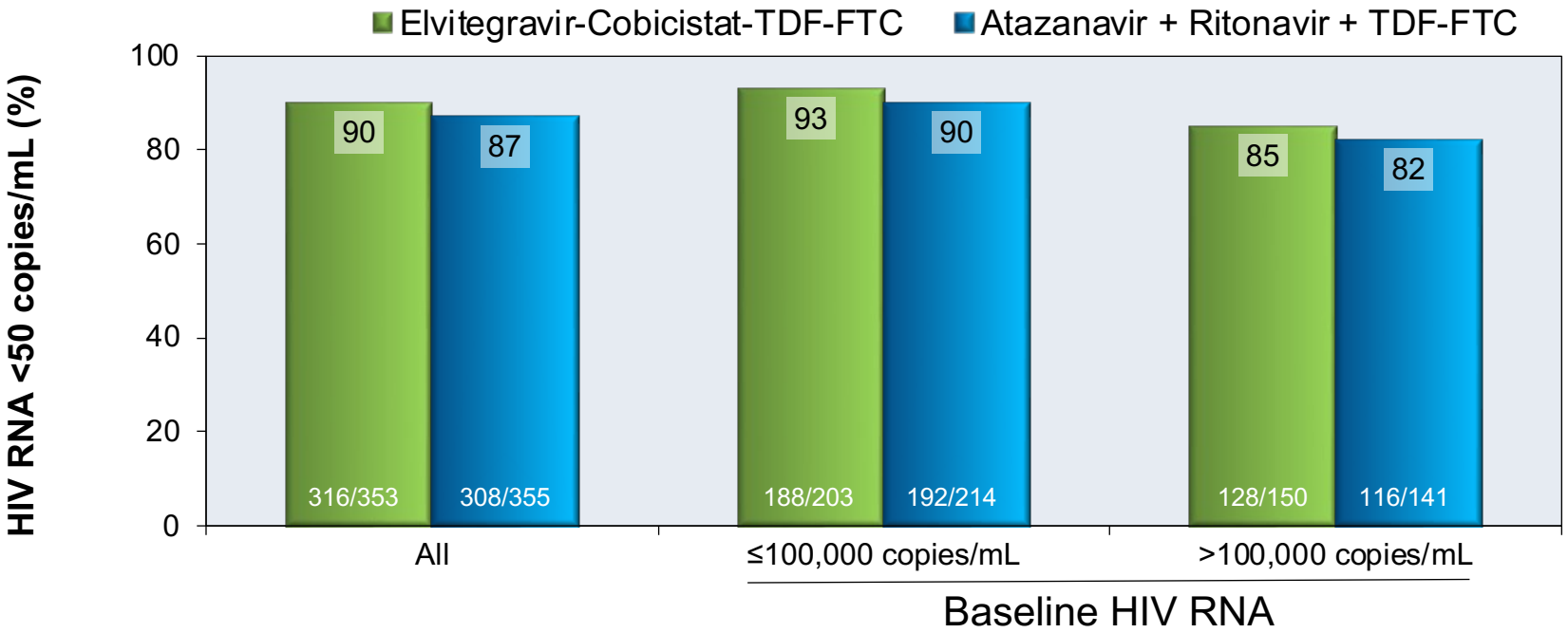
- **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir-emtricitabine with atazanavir + ritonavir + tenofovir DF-emtricitabine
- **Inclusion Criteria** (n = 708)
  - Antiretroviral-naïve adults
  - Age ≥18 years
  - HIV RNA ≥5,000 copies/mL
  - Any CD4 count
- **Treatment Arms**
  - Elvitegravir-Cobicistat-TDF-FTC
  - Atazanavir + RTV + TDF-FTC



Source: DeJesus E, et al. Lancet. 2012;379:2429-38.

Elvitegravir-Cobicistat-TDF-FTC versus Atazanavir + RTV + TDF-FTC Study 103: Results

Week 48 Virologic Response



Source: DeJesus E, et al. Lancet. 2012;379:2429-38.
DeJesus E, et al. 19th IAC. 2012; Abstract TUPE43.

Elvitegravir-Cobicistat-TDF-FTC versus Atazanavir + RTV + TDF-FTC Study 103: Common Adverse Events

Treatment Emergent Adverse Events in ≥ 10% of Subjects in Either Group		
	EVG-COBI-TDF-FTC (n = 353)	**ATV + RTV + TDF-FTC** (n= 355)
Diarrhea	22%	27%
Nausea*	20%	19%
Upper Respiratory Tract Infection	15%	16%
Headache	15%	12%
Fatigue	14%	13%
Ocular Icterus*	1%	14%

*$p < 0.001$

Source: DeJesus E, et al. Lancet. 2012;379:2429-38.

Elvitegravir-Cobicistat-TDF-FTC versus Atazanavir + RTV + TDF-FTC Study 103: Conclusions

Interpretation: “This study met the primary endpoint of non-inferiority of elvitegravir/cobicistat/emtricitabine/tenofovir (EVG/COBI/FTC/TDF) to atazanavir plus ritonavir plus emtricitabine/tenofovir (ATV + RTV + FTC/TDF) and demonstrates the robust antiviral efficacy of the only integrase inhibitor-based single tablet regimen for initial HIV treatment.”

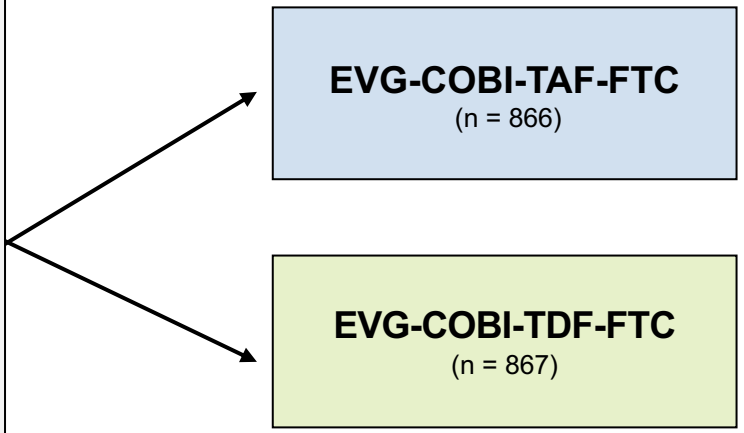
Source: DeJesus E, et al. Lancet. 2012;379:2429-38.

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

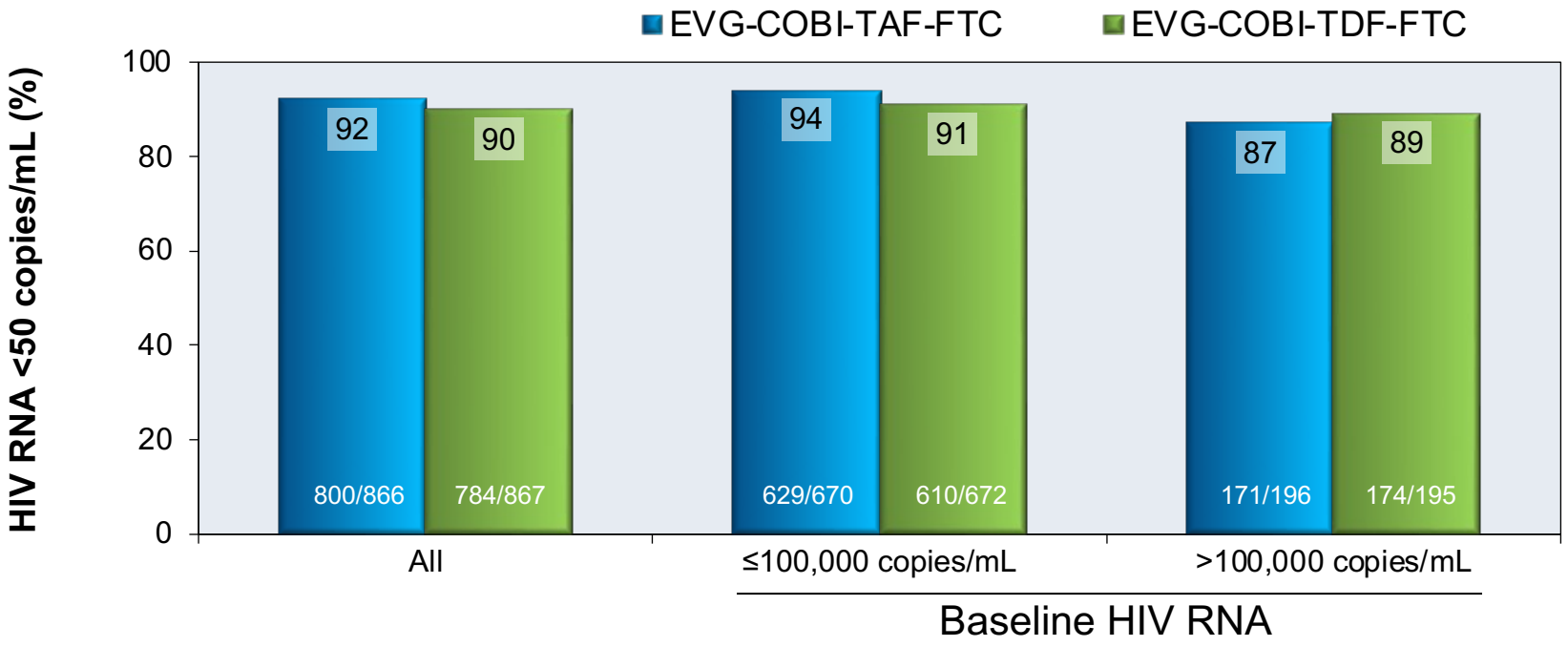
- **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine with elvitegravir-cobicistat-tenofovir DF-emtricitabine
- **Inclusion Criteria** (n = 1,733)
  - Antiretroviral-naïve patients
  - Age >18
  - HIV RNA ≥1000 copies/mL
  - Any 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

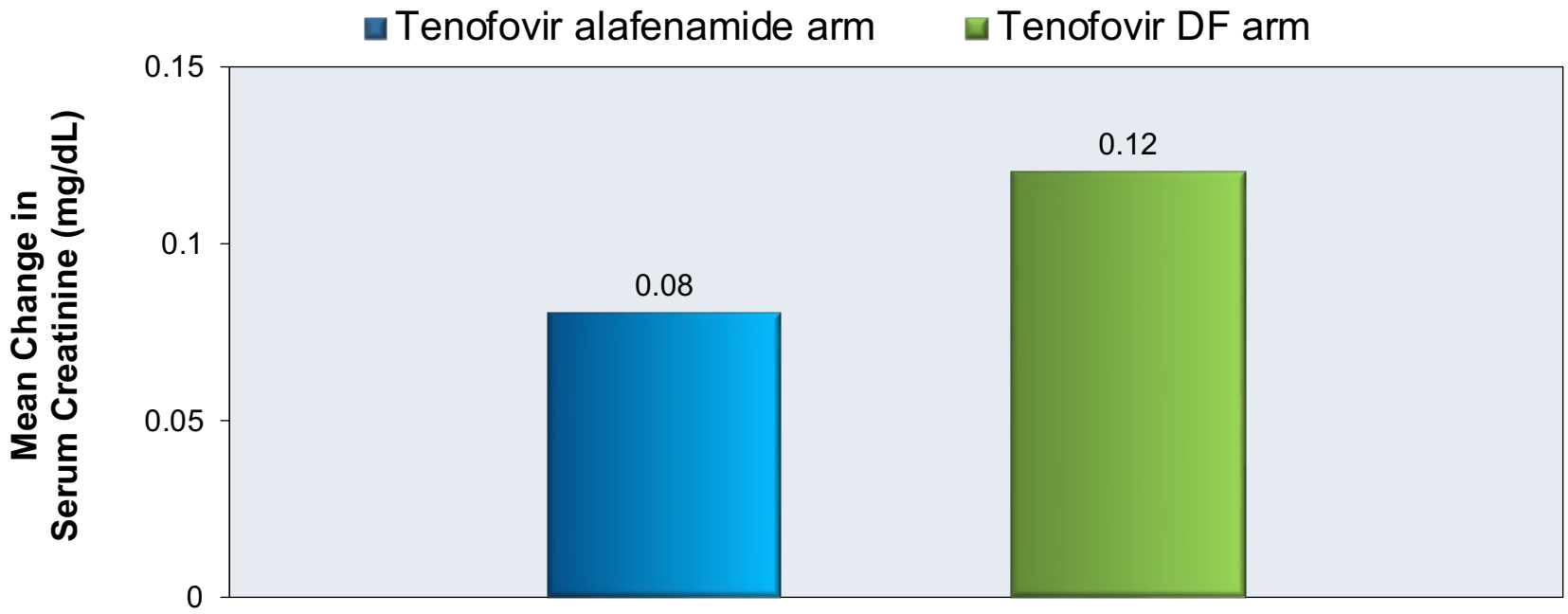


Source: Sax PE, et al. Lancet. 2015;385:2606-15.

National HIV Curriculum

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

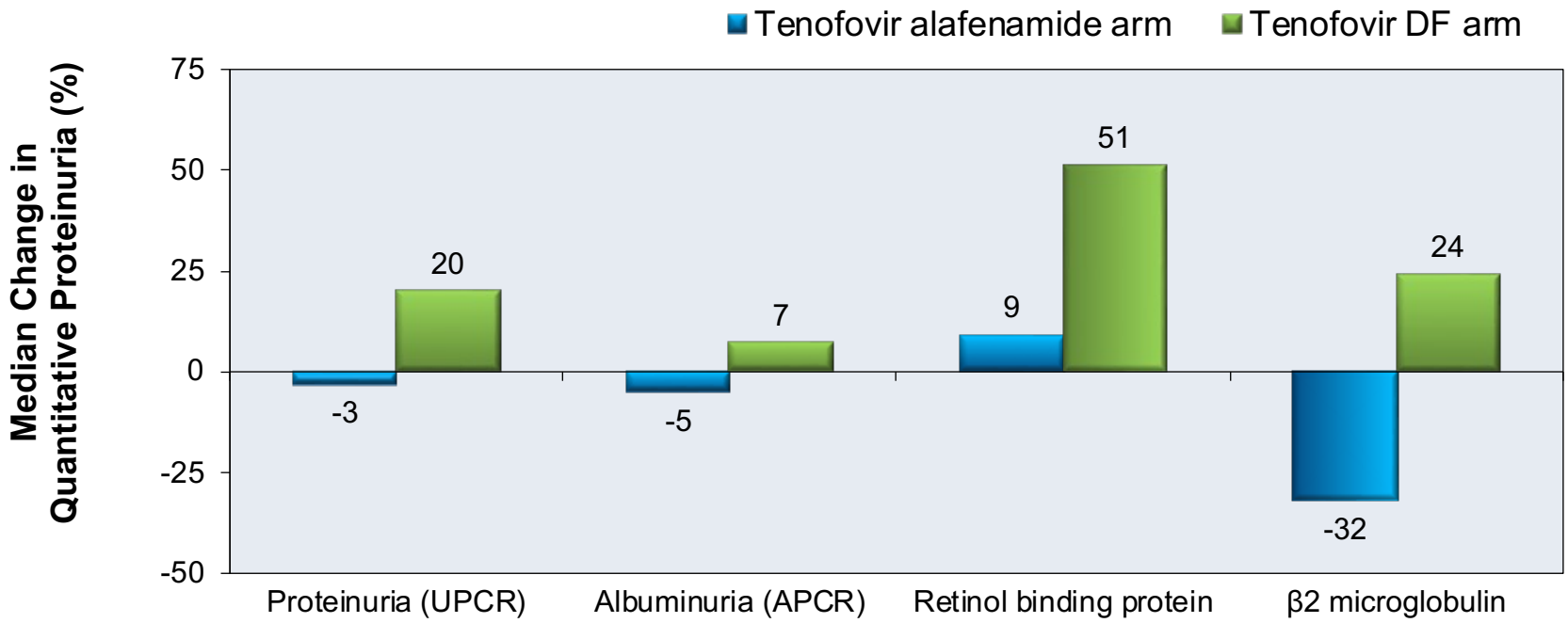
Week 48 Change in Serum Creatinine from Baseline



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

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

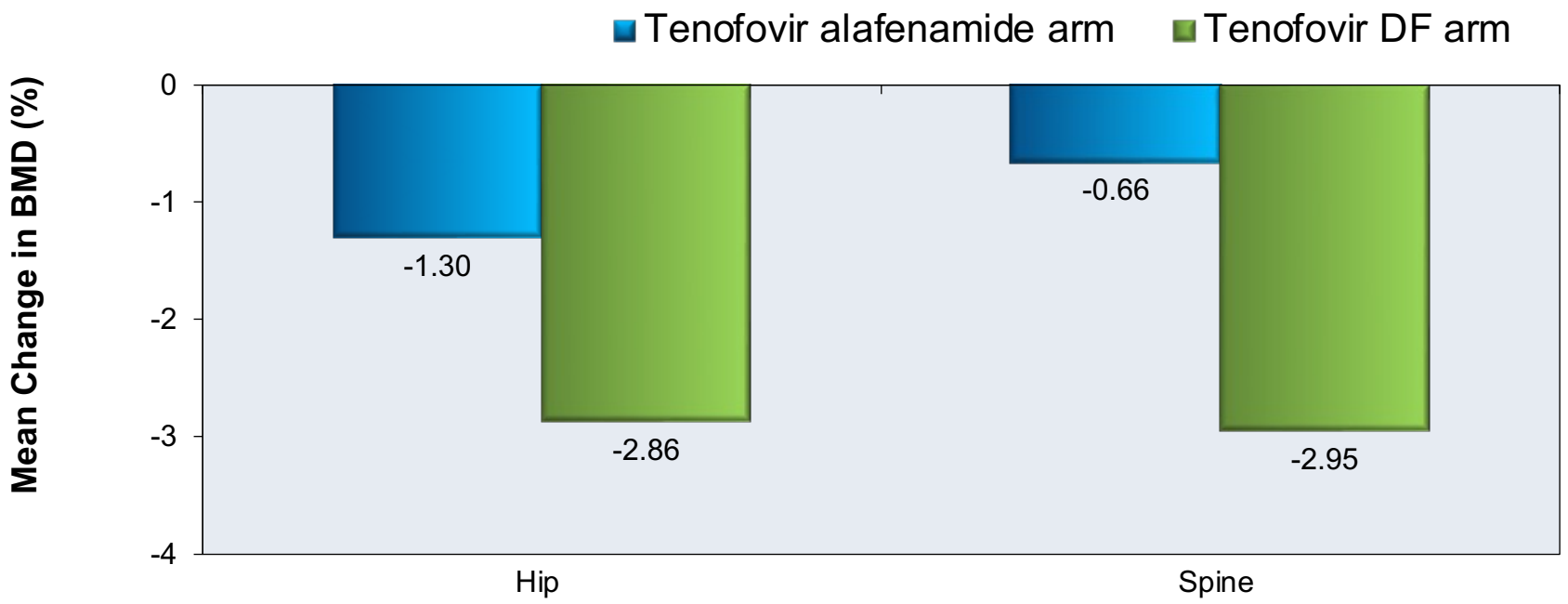
Week 48 Changes in Quantitative Proteinuria from Baseline



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.”

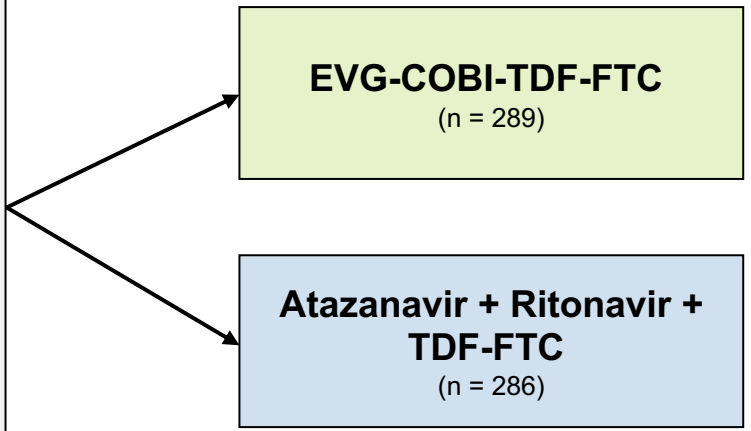
Source: Sax PE, et al. Lancet. 2015;385:2606-15.

EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC in Women

Study 128 (WAVES)

EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC (in Women)
WAVES Study: Design

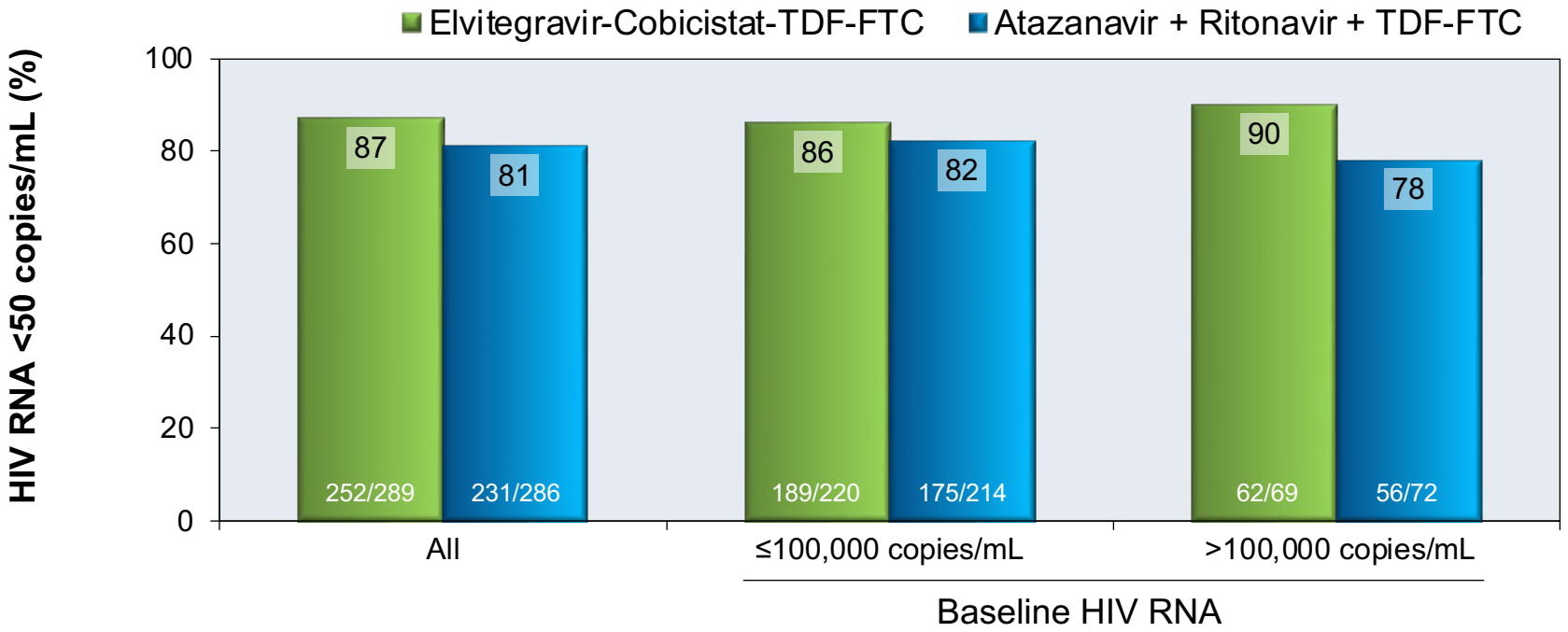
- **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir-emtricitabine with atazanavir + ritonavir + tenofovir DF-emtricitabine in women
- **Inclusion Criteria** (n = 575)
  - Antiretroviral-naïve women
  - Age ≥18 years
  - HIV RNA ≥500 copies/mL
  - Any CD4 count
- **Treatment Arms**
  - Elvitegravir-Cobicistat-TDF-FTC
  - Atazanavir + Ritonavir + TDF-FTC



Source: Squires L, et al. Lancet HIV. 2016;3:e410-20.

EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC (in Women) WAVES Study: Result

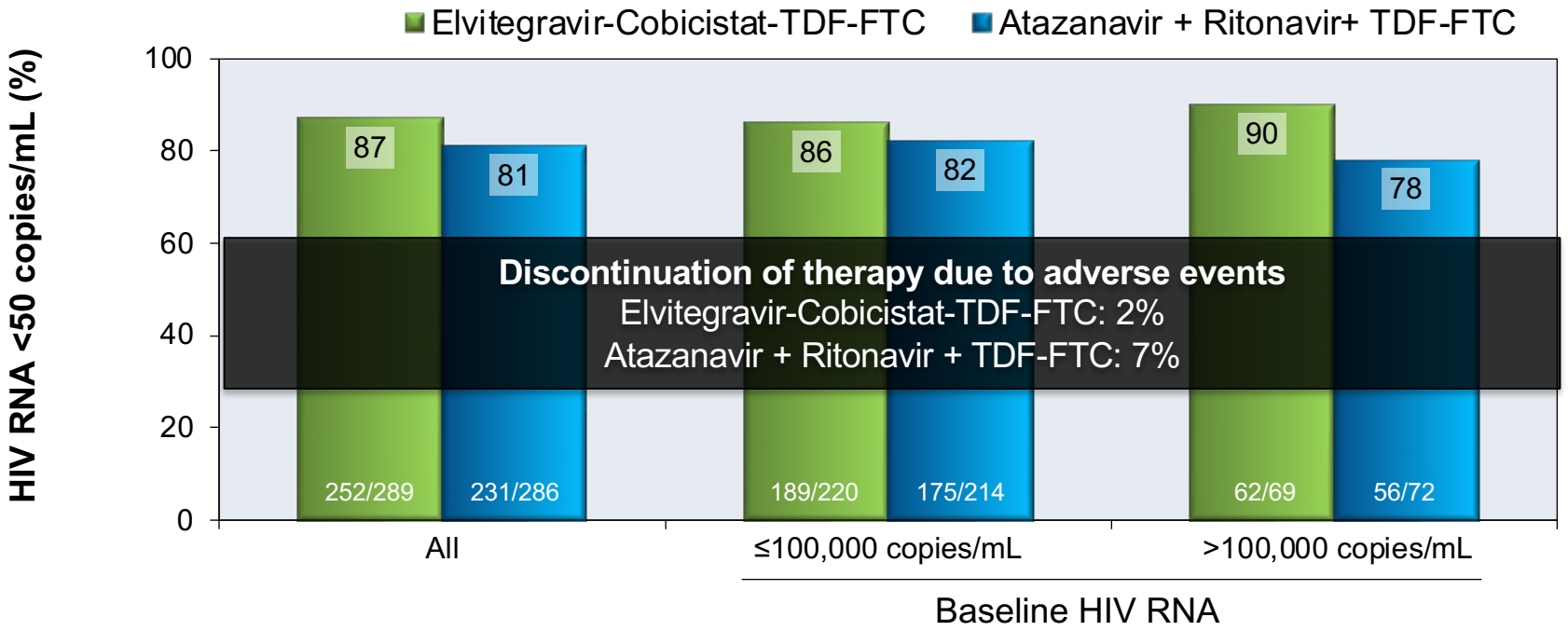
Week 48 Virologic Response



Source: Squires L, et al. Lancet HIV. 2016;3:e410-20.

EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC (in Women) WAVES Study: Result

Week 48 Virologic Response



Source: Squires L, et al. Lancet HIV. 2016;3:e410-20.

EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC (in Women) WAVES Study: Common Adverse Events

Treatment Emergent Adverse Events in ≥ 10% of Subjects in Either Group		
	EVG-COBI-TDF-FTC (n = 289)	**ATV + RTV + TDF-FTC** (n= 286)
Headache	16%	15%
Upper Respiratory Tract Infection	16%	15%
Malaria	11%	8%
Nausea	15%	14%
Vomiting	10%	6%
Jaundice	<1%	11%
Icterus	<1%	12%

Source: Squires L, et al. Lancet HIV. 2016;3:e410-20.

EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC (in Women)
WAVES Study: Conclusions

Interpretation: “WAVES shows that clinical trials of ART regimens in global and diverse populations of treatment-naive women are possible. The findings support guidelines recommending integrase inhibitor based regimens in first-line antiretroviral therapy.”

Source: Squires L, et al. Lancet HIV. 2016;3:e410-20.

Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

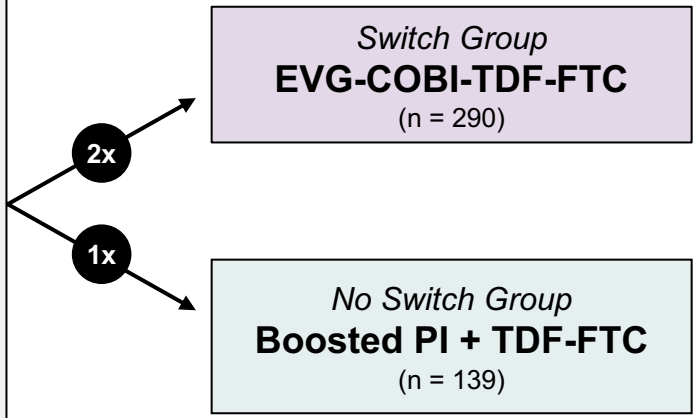
Switch Studies

Switch from PI-Based Regimen to EVG-COBI-TDF-FTC

Study 115 (STRATEGY-PI)

Switch from PI-Based Regimen to EVG-COBI-TDF-FTC
STRATEGY-PI: Design

- **Background**: Open-label, randomized, phase 3b trial comparing switch to elvitegravir-cobicistat-tenofovir DF-emtricitabine versus continuation of baseline regimen of ritonavir + PI + tenofovir DF-emtricitabine
- **Inclusion Criteria** (n = 433)
  - HIV RNA <50 copies/mL on ART for ≥6 months
  - Baseline regimen of RTV + PI + TDF-FTC
  - No prior virologic failure
  - No resistance to TDF or FTC
  - CrCl ≥70 mL/min
- **Treatment Arms**
  - EVG-COBI-TDF-FTC (Switch group)
  - Remain on RTV + PI + TDF-FTC (No switch group)

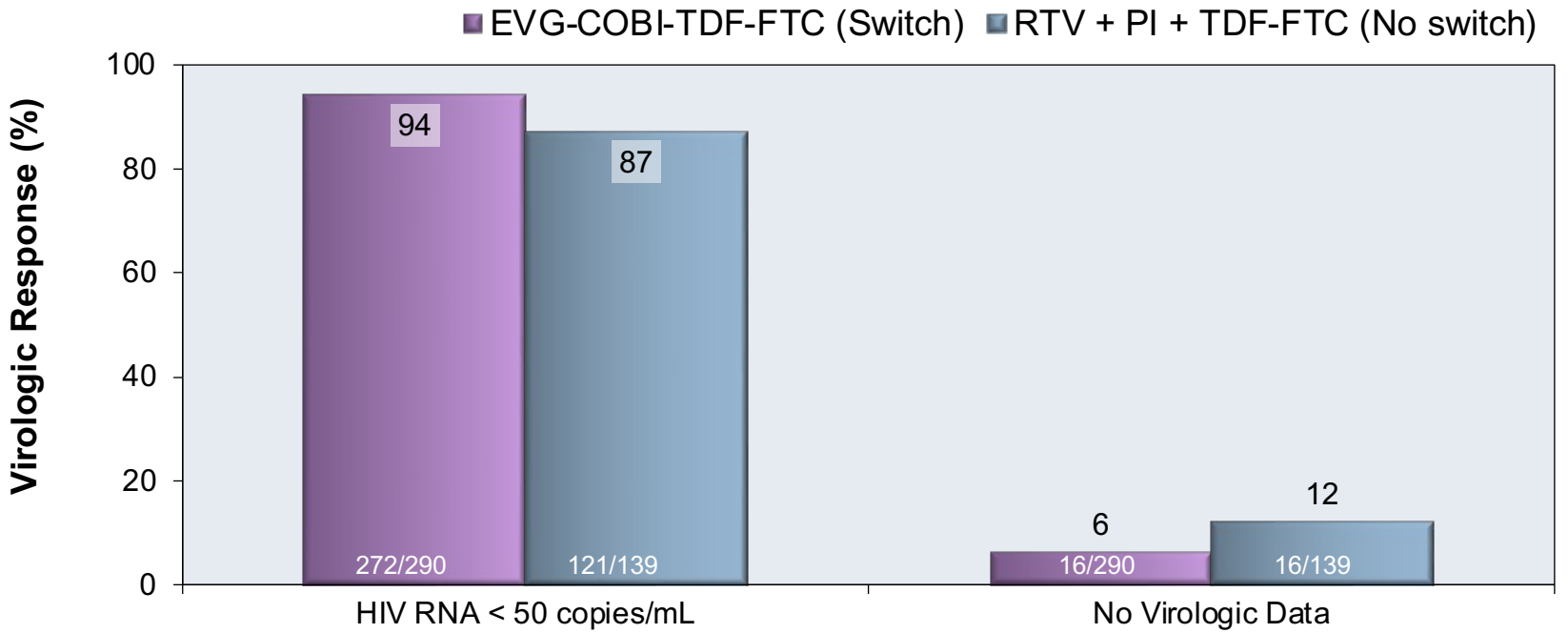


*__NOTE:__ 3 participants from switch group and 1 from no switch group were excluded from study after screening for protocol violations.

Source: Arribas JR, et al. Lancet Infect Dis. 2014;14:581-9.

Switch from PI-Based Regimen to EVG-COBI-TDF-FTC STRATEGY-PI: Result

Week 48 Virologic Response



Source: Arribas JR, et al. Lancet Infect Dis. 2014;14:581-9.

Switch from PI-Based Regimen to EVG-COBI-TDF-FTC
STRATEGY-PI: Study Conclusions

Interpretation: “Coformulated elvitegravir, cobicistat, emtricitabine, and tenofovir might be a useful regimen simplification option for virologically suppressed adults with HIV taking a multi-tablet ritonavir-boosted protease inhibitor regimen.”

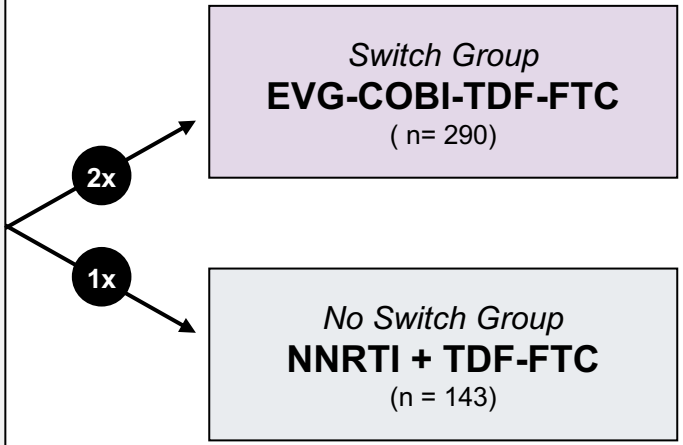
Source: Arribas JR, et al. Lancet Infect Dis. 2014;14:581-9.

Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC

Study 121 (STRATEGY-NNRTI)

Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC
STRATEGY-NNRTI: Design

- **Background**: Open-label, randomized, phase 3b trial comparing switch to elvitegravir-cobicistat-tenofovir DF-emtricitabine versus continuation of baseline regimen of NNRTI + TDF-FTC
- **Inclusion Criteria** (n = 439)
  - HIV RNA <50 copies/mL on ART for ≥6 months
  - Baseline regimen of NNRTI + TDF-FTC
  - No prior virologic failure
  - No resistance to TDF or FTC
  - CrCl ≥70 mL/min
- **Treatment Arms**
  - EVG-COBI-FTC-TDF (Switch group)
  - Remain on NNRTI + FTC-TDF (No switch group)

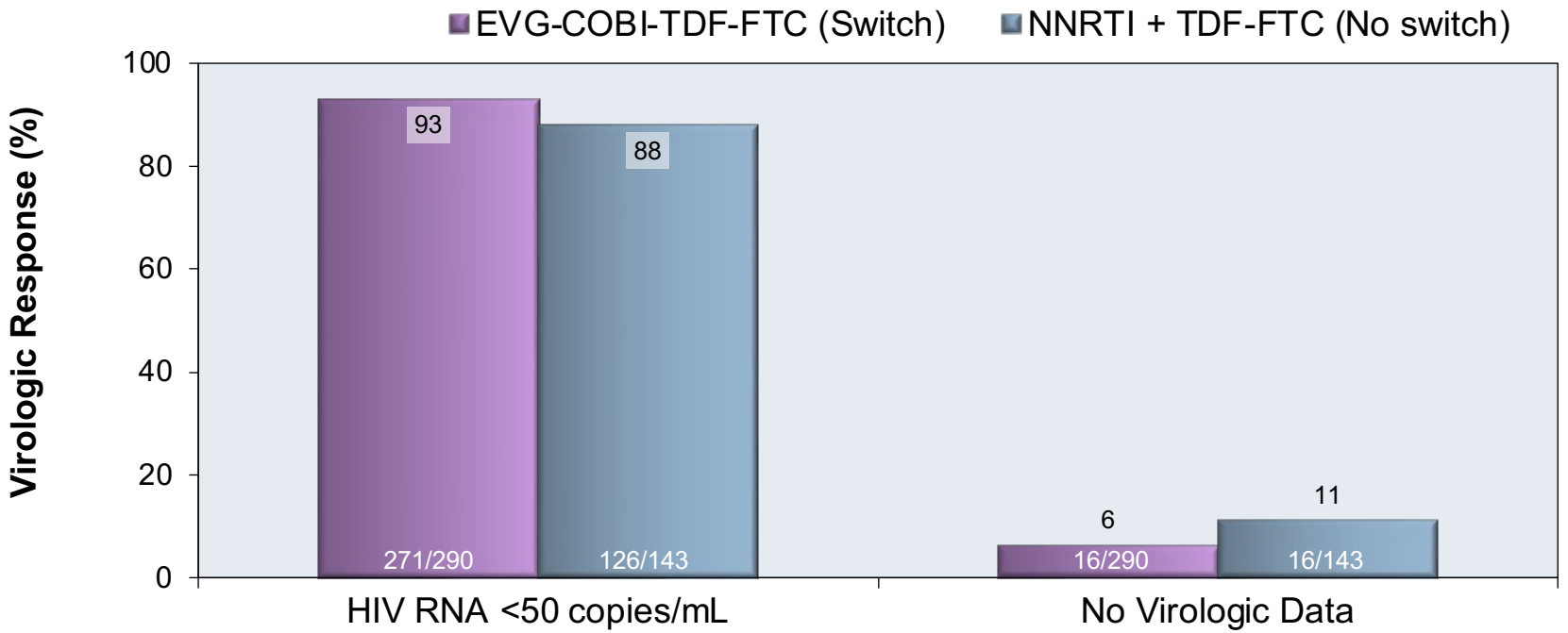


***NOTE**: 2 participants from switch group and 4 participants from no-switch group were excluded from the study after screening (2 protocol violation,1 non-adherence, 3 withdrew consent)

Source: Pozniak A, et al. Lancet Infect Dis. 2014;14:590-9

Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC STRATEGY-NNRTI: Results

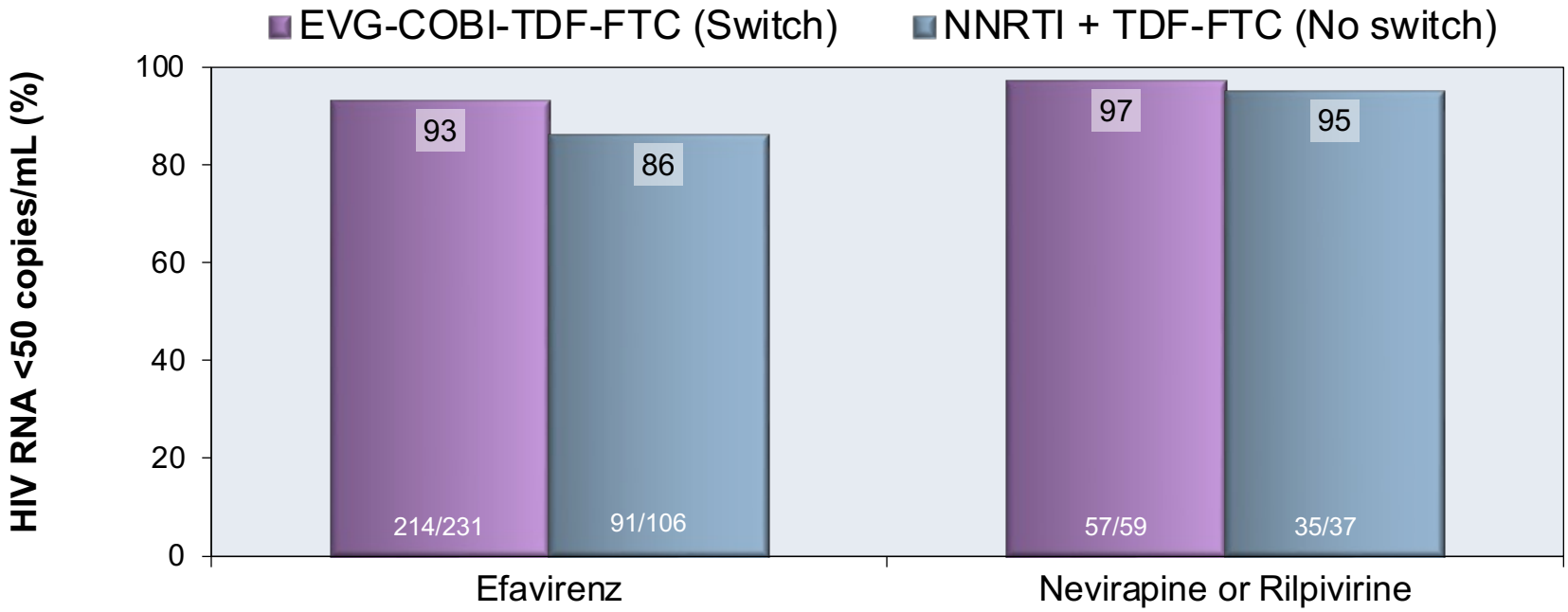
Week 48 Virologic Response



Source: Pozniak A, et al. Lancet Infect Dis. 2014;14:590-9

Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC STRATEGY-NNRTI: Results

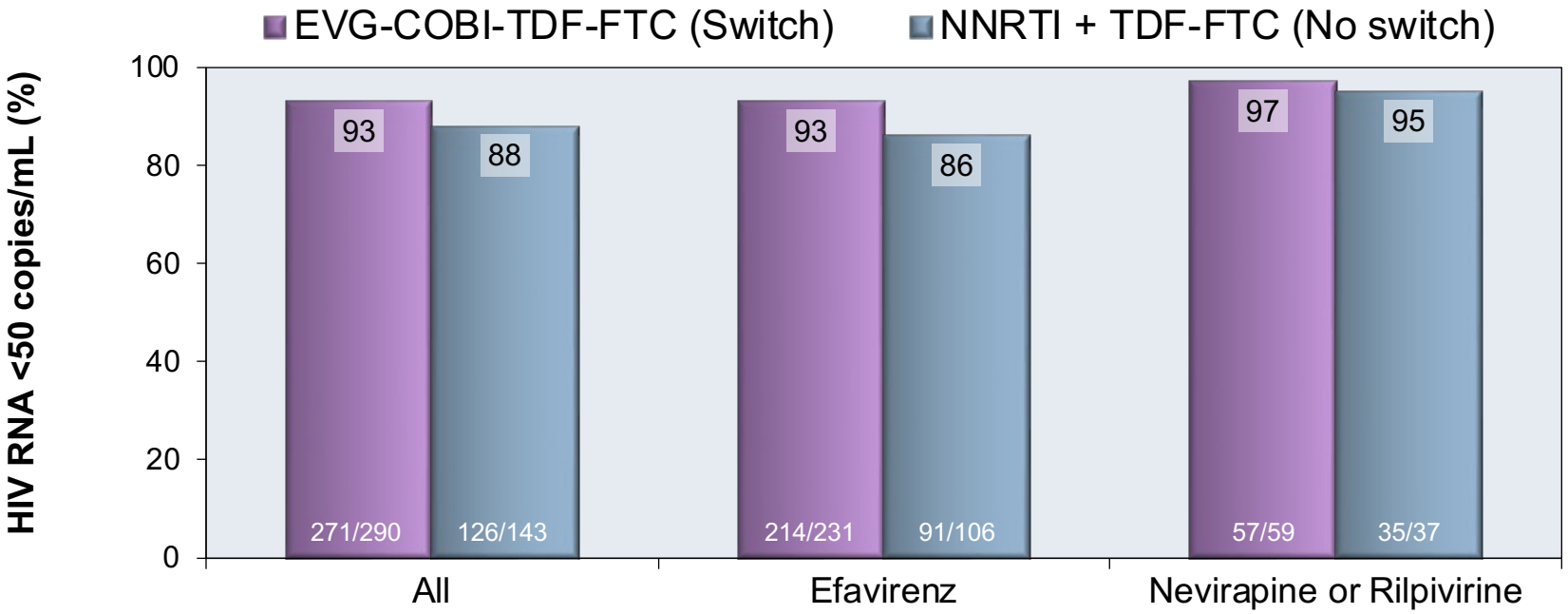
Week 48 Virologic Response, Subgroup Analysis, by Baseline NNRTI Regimen



Source: Pozniak A, et al. Lancet Infect Dis. 2014;14:590-9

Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC STRATEGY-NNRTI: Results

Week 48 Virologic Response, Subgroup Analysis, by Baseline NNRTI Regimen



Source: Pozniak A, et al. Lancet Infect Dis. 2014;14(7):590-9

Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC STRATEGY-NNRTI: Conclusions

Interpretation: “Coformulated elvitegravir, cobicistat, emtricitabine, and tenofovir seems to be efficacious and well tolerated in virologically suppressed adults with HIV and might be a suitable alternative for patients on an NNRTI with emtricitabine and tenofovir regimen considering a regimen modification or simplification.”

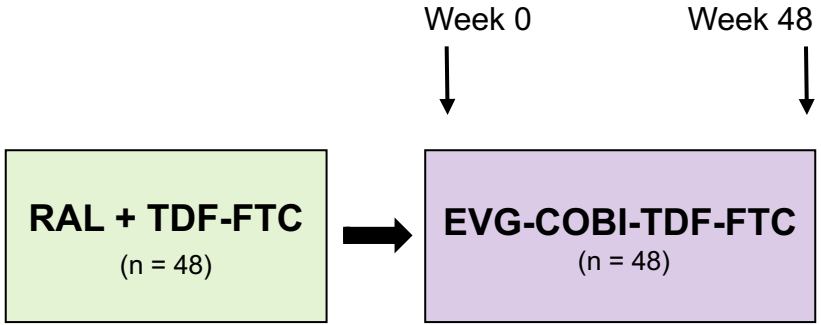
Source: Pozniak A, et al. Lancet Infect Dis. 2014;14:590-9.

Switch to Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

Study 123

Switch to Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine Study 123: Study Design

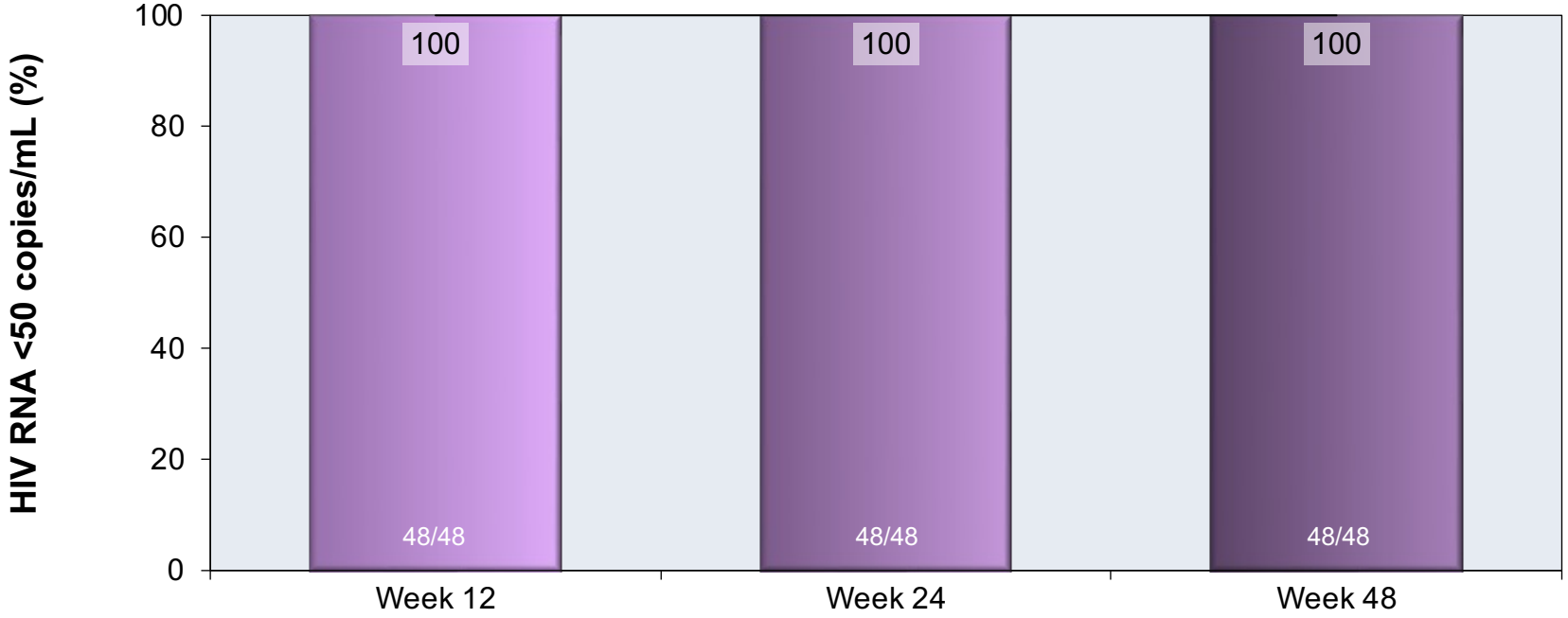
- **Background**: Open-label, randomized phase 3b trial evaluating switching to once-daily elvitegravir-cobicistat-tenofovir DF-emtricitabine from twice daily raltegravir plus tenofovir DF-emtricitabine
- **Inclusion Criteria** (n = 48)
  - HIV RNA <50 copies/mL
  - On RAL+ TDF-FTC for ≥6 months
  - Not taking any other ART
  - No new AIDS-defining conditions
- **Treatment Arms**
  - Switch to EVG-COBI-TDF-FTC



Source: Mills A, et al. HIV Clin Trials. 2014;15:51-6.

Switch to Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine Study 123: Results

Virologic Response After Switch to EVG-COBI-TDF-FTC



Source: Mills A, et al. HIV Clin Trials. 2014;15:51-6.

Switch to Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine
Study 123: Common Adverse Events

Treatment Emergent Adverse Events in ≥ 10% of Subjects	
Adverse Event (treatment emergent)	**Switched to EVG-COBI-TDF-FTC** (n = 48)
Upper Respiratory Tract Infection	21%
Insomnia	13%
Diarrhea	10%
Fatigue	10%
Anxiety	10%

Source: Mills A, et al. HIV Clin Trials. 2014;15:51-6.

Switch to Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine
Study 123: Conclusions

Conclusion: “All participants switching to 1 tablet once-a-day elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (*Stribild*) from a twice-daily raltegravir + emtricitabine/tenofovir disoproxil fumarate regimen remained virologically suppressed. *Stribild* was well tolerated. Switching to *Stribild* may be a viable option for virologically suppressed patients wanting to simplify from a twice-daily raltegravir-containing regimen.”

Source: Mills A, et al. HIV Clin Trials. 2014;15:51-6.

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