National HIV Curriculum

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

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AETC AIDS Education & Training Center Program

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

**Stribild**

[STRY-bild]


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*)

- ***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

# Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine Summary of Key Studies

- Phase 2 Trials in Treatment Naïve
  - GS-236-104: EVG-COBI-TDF-FTC vs. EFV-TDF-FTC
  - GS-236-104: EVG-COBI-TDF-FTC vs. EFV-TDF-FTC
- Phase 3 Trials in Treatment Naïve
  - Study 102: EVG-COBI-TDF-FTC vs. EFV-TDF-FTC
  - Study 103: EVG-COBI-TDF-FTC vs. RTV + ATZ + TDF-FTC
  - Study 104 and Study 111: EVG-COBI-TAF-FTC vs. EVG-COBI-TDF-FTC
  - Study 128 (WAVES): EVG-COBI-TDF-FTC vs. RTV + ATZ + TDF-FTC
- Phase 3b 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

INITIAL THERAPY

# Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

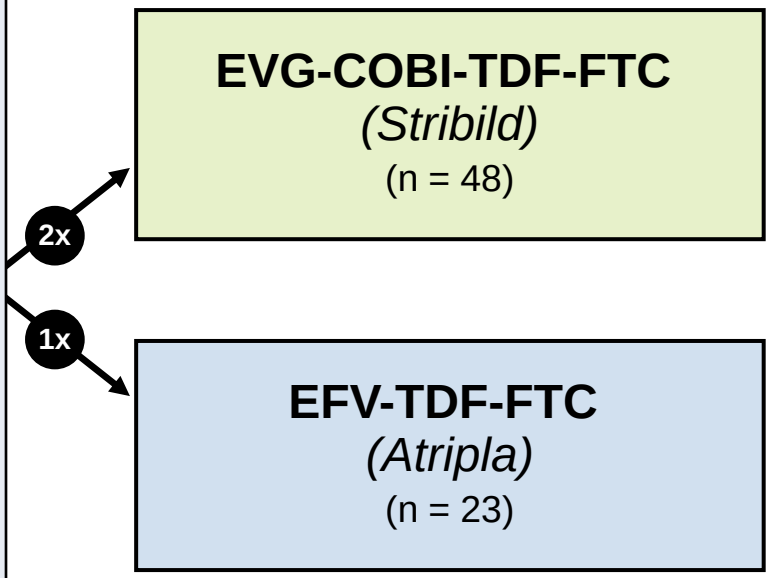
Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC

# GS-236-104

# Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC
# GS-236-104: Design

## Study Design: Study 236-104

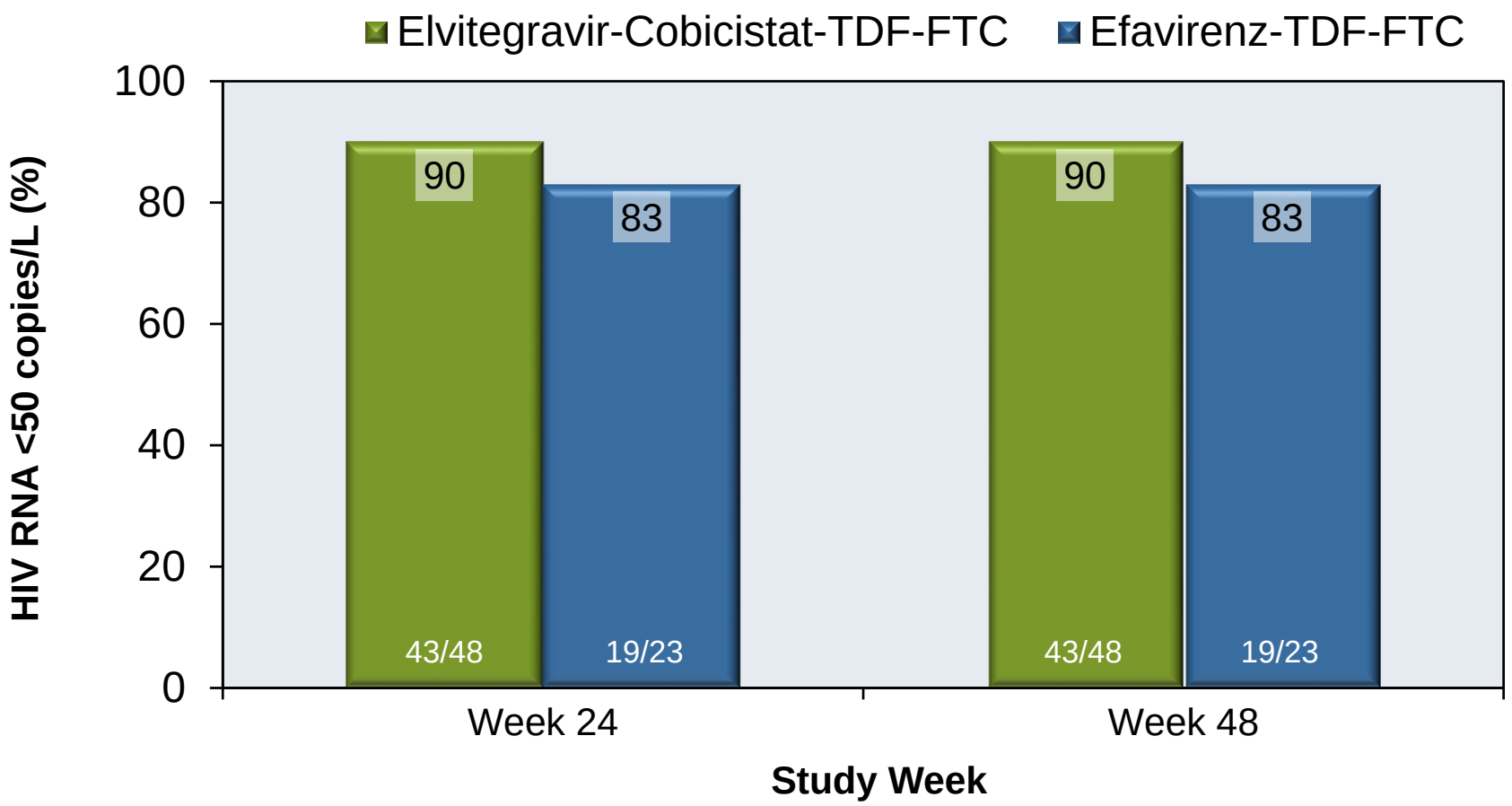
- **Background**: Randomized, double-blind, double dummy, phase 2 trial comparing elvitegravir-cobicistat-tenofovir DF-emtricitabine with efavirenz-tenofovir DF-emtricitabine
- **Inclusion Criteria (n = 71)**
  - Antiretroviral-naïve adults
  - Age ≥18
  - HIV RNA ≥5,000 copies/ml
  - CD4 count >50 cells/mm$^3$
- **Treatment Arms**
  - Elvitegravir-cobicistat-tenofovir DF-emtricitabine
  - Efavirenz-tenofovir DF-emtricitabine




Source: Cohen C, et al. AIDS. 2011;25:F7-12.

# Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC
# GS-236-104: Results

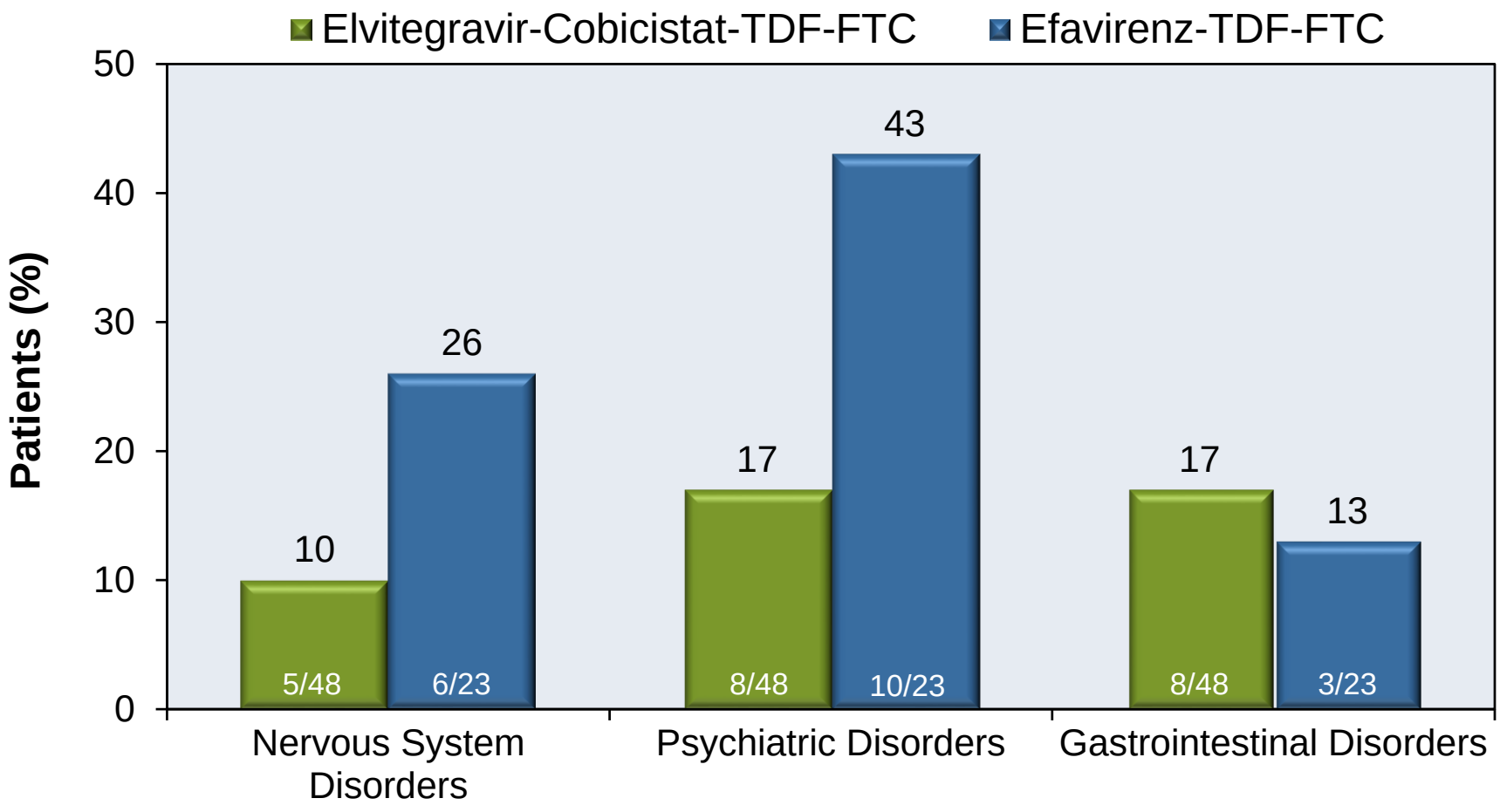
## Week 24 and 48: Virologic Response ( ITT Analysis, M=F)




Source: Cohen C, et al. AIDS. 2011;25:F7-12.

# Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC
# GS-236-104: Adverse Effects

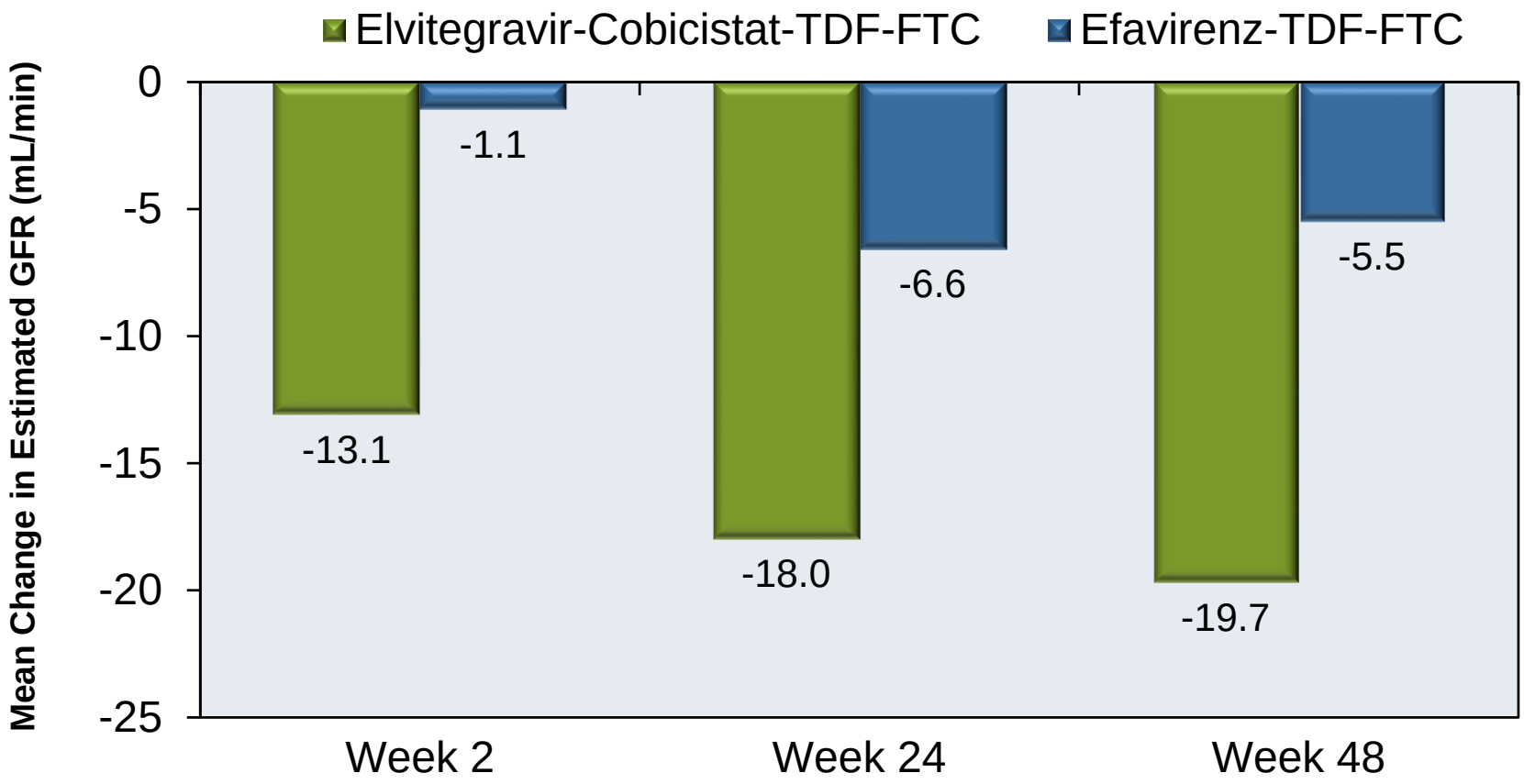
## Drug-Related, Treatment-Emergent Adverse Effects




**Source: Cohen C, et al. AIDS. 2011;25:F7-12.**

# Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC
# GS-236-104: Adverse Effects

## Change in Estimated Glomerular Filtration Rate (Cockcroft-Gault)




**Source: Cohen C, et al. AIDS. 2011;25:F7-12.**

# Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC
# GS-236-104: Conclusions

**Conclusion**: “Once-daily elvitegravir/cobicistat/emtricitabine/tenofovir (EVG/COBI/FTC/TDF) achieved and maintained a high rate of virologic suppression with fewer central nervous system and psychiatric adverse events compared to a current standard-of-care regimen of efavirenz/emtricitabine/tenofovir DF (EFV/FTC/TDF).”

**Source: Cohen C, et al. AIDS. 2011;25:F7-12.**

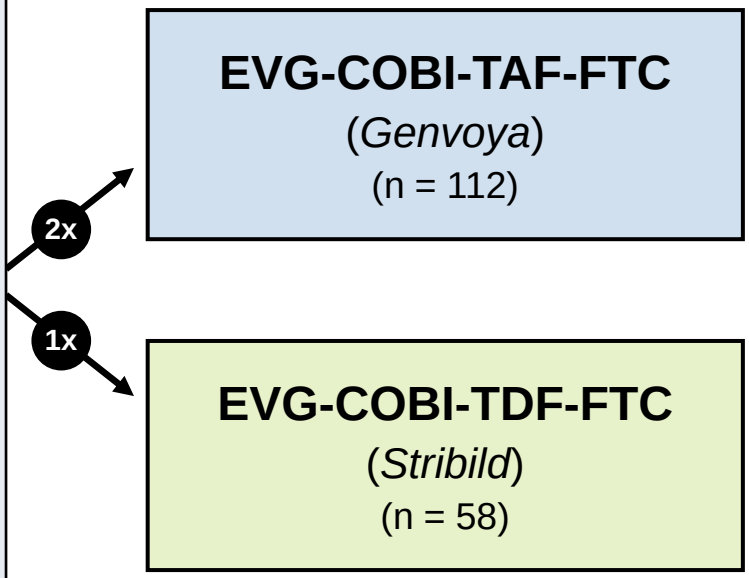
EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC

# GS-292-0102 Study

# EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
# GS-292-102 Study: Design

## Study Design: GS-292-0102

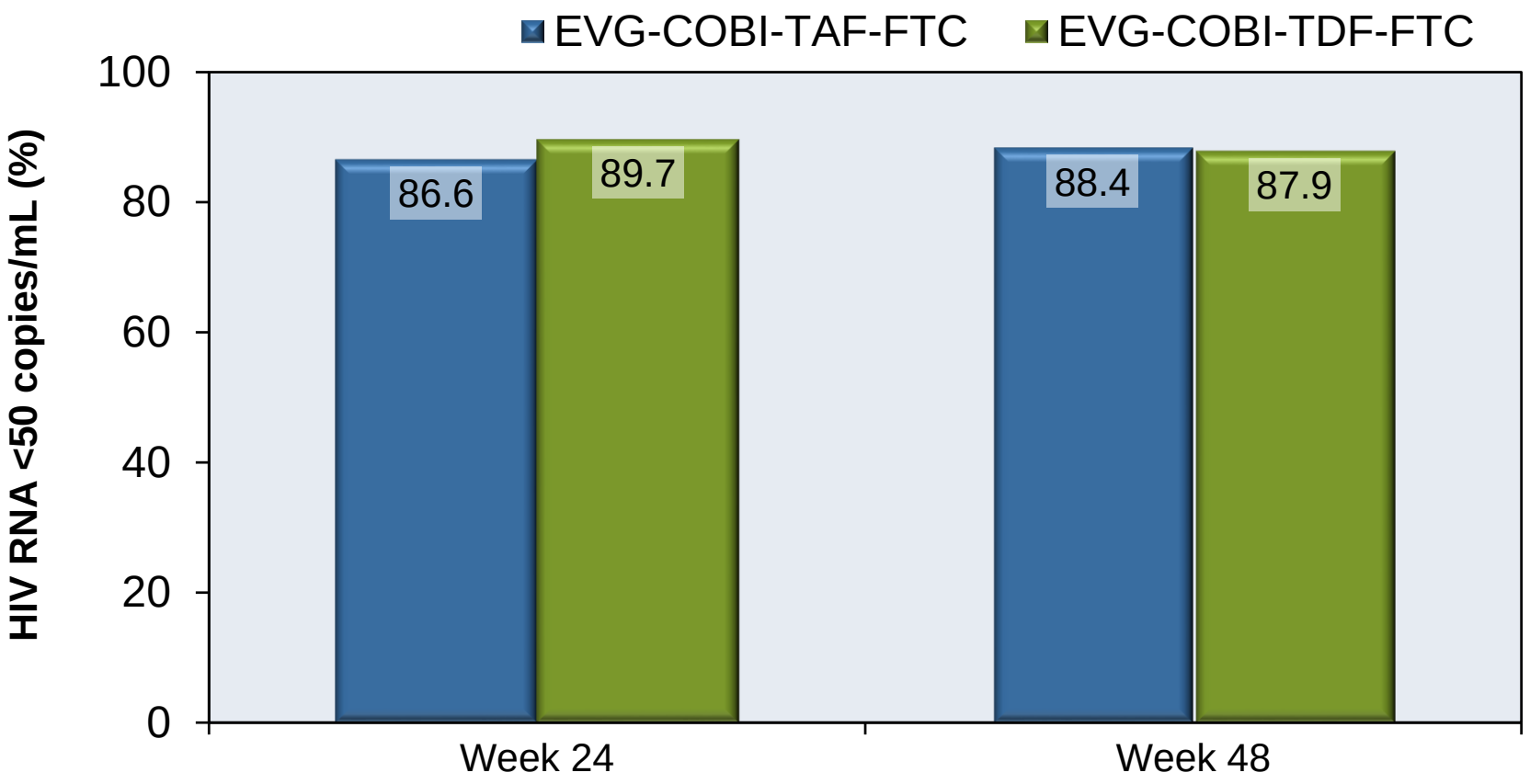
- **Background**: Randomized, double-blind, phase 2 trial comparing elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine with elvitegravir-cobicistat-tenofovir DF-emtricitabine
- **Inclusion Criteria (n = 171 randomized)**
  - Antiretroviral-naïve adults
  - Age ≥18
  - HIV RNA ≥5000 copies/mL
  - CD4 count >50 cells/mm$^3$
  - Estimated GFR ≥70 mL/min
  - No AIDS conditions in prior 30 days
  - Excluded if coinfected with HBV or HCV
- **Treatment Arms**
  - Elvitegravir-Cobicistat-TAF-FTC
  - Elvitegravir-Cobicistat-TDF-FTC




**Source: Sax PE, et al. J Acquir Immune Defic Syndr. 2014;67:52-8.**

# EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
# GS-292-102 Study: Results

## Week 24 and 48 Virologic Response (Snapshot Analysis)




Source: Sax PE, et al. J Acquir Immune Defic Syndr. 2014;67:52-8.

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# EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
# GS-292-0102 Study: Conclusions

**Conclusions**: “Treatment-naive patients given the STR that contained either TAF or TDF achieved a high rate of virologic success. Compared with those receiving TDF, patients on E/C/F/TAF experienced significantly smaller changes in estimated creatinine clearance, renal tubular proteinuria, and bone mineral density.”

**Source: Sax PE, et al. J Acquir Immune Defic Syndr. 2014;67:52-8.**

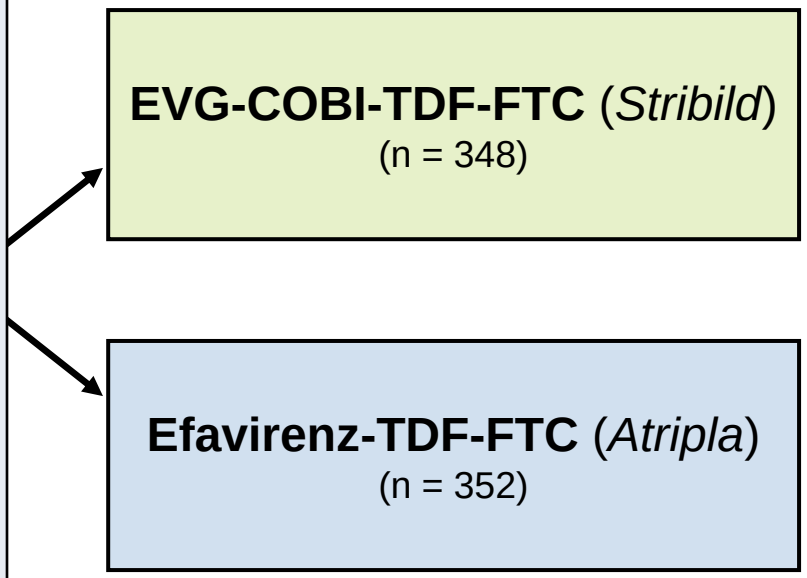
Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC

# Study 102

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

**Study Design: Study 102**

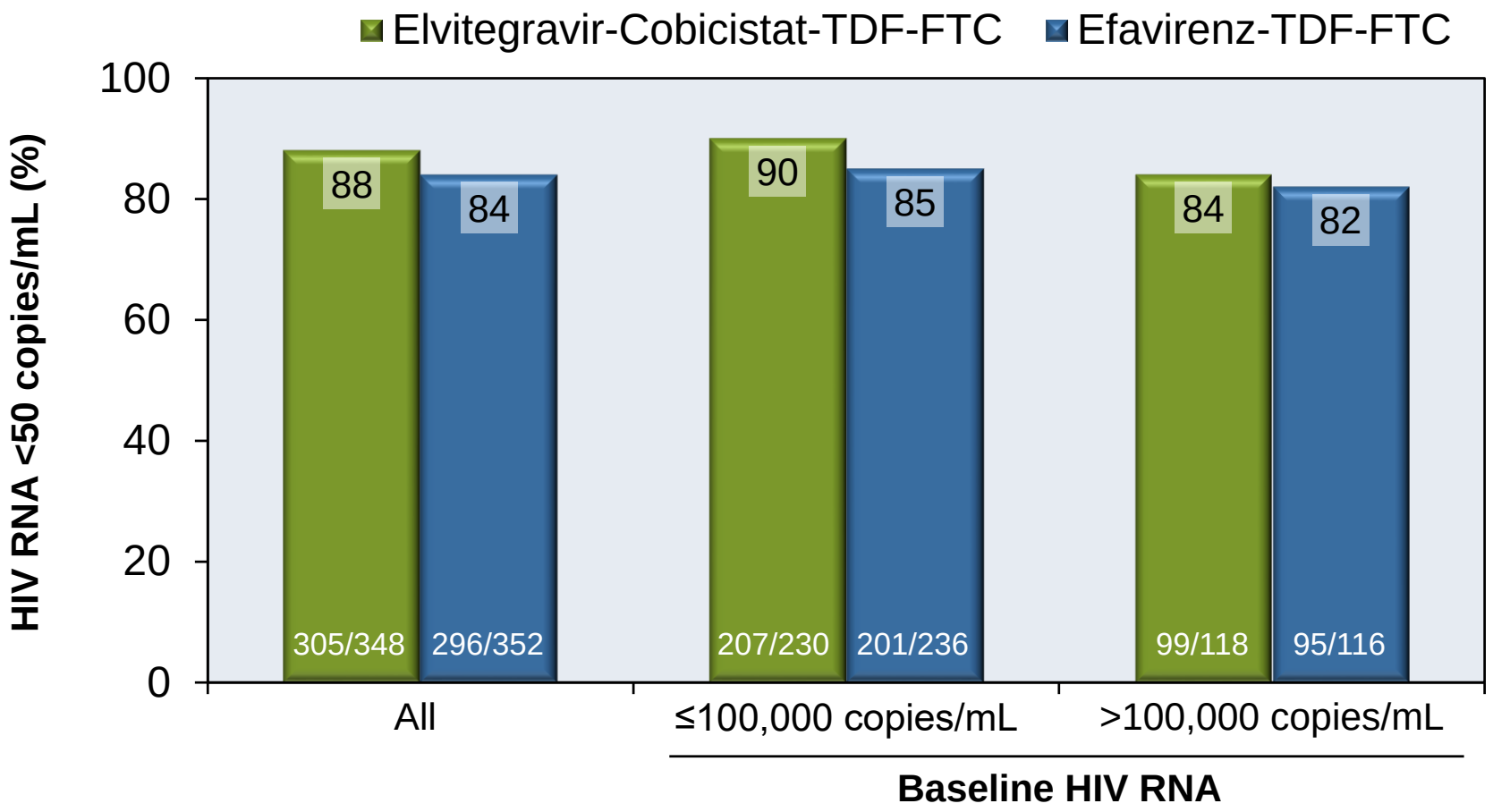
- **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir DF-emtricitabine with efavirenz-tenofovir DF-emtricitabine
- **Inclusion Criteria (n = 700)**
  - Antiretroviral-naïve adults
  - Age ≥18
  - HIV RNA ≥5,000 copies/mL
  - No AIDS conditions in previous 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: Snapshot Analysis (ITT, Missing=Failure)




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

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# 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.**

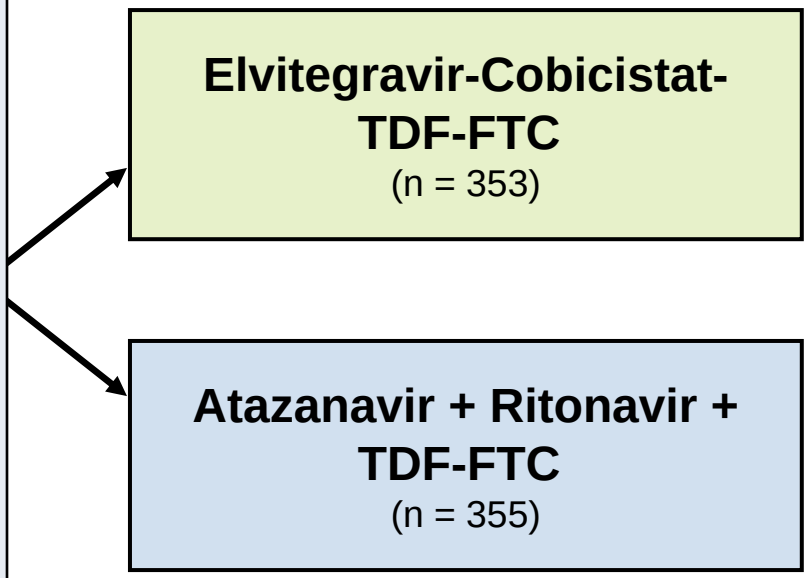
EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC

# Study 103

# Study 103: Design

## Study Design: Study 103

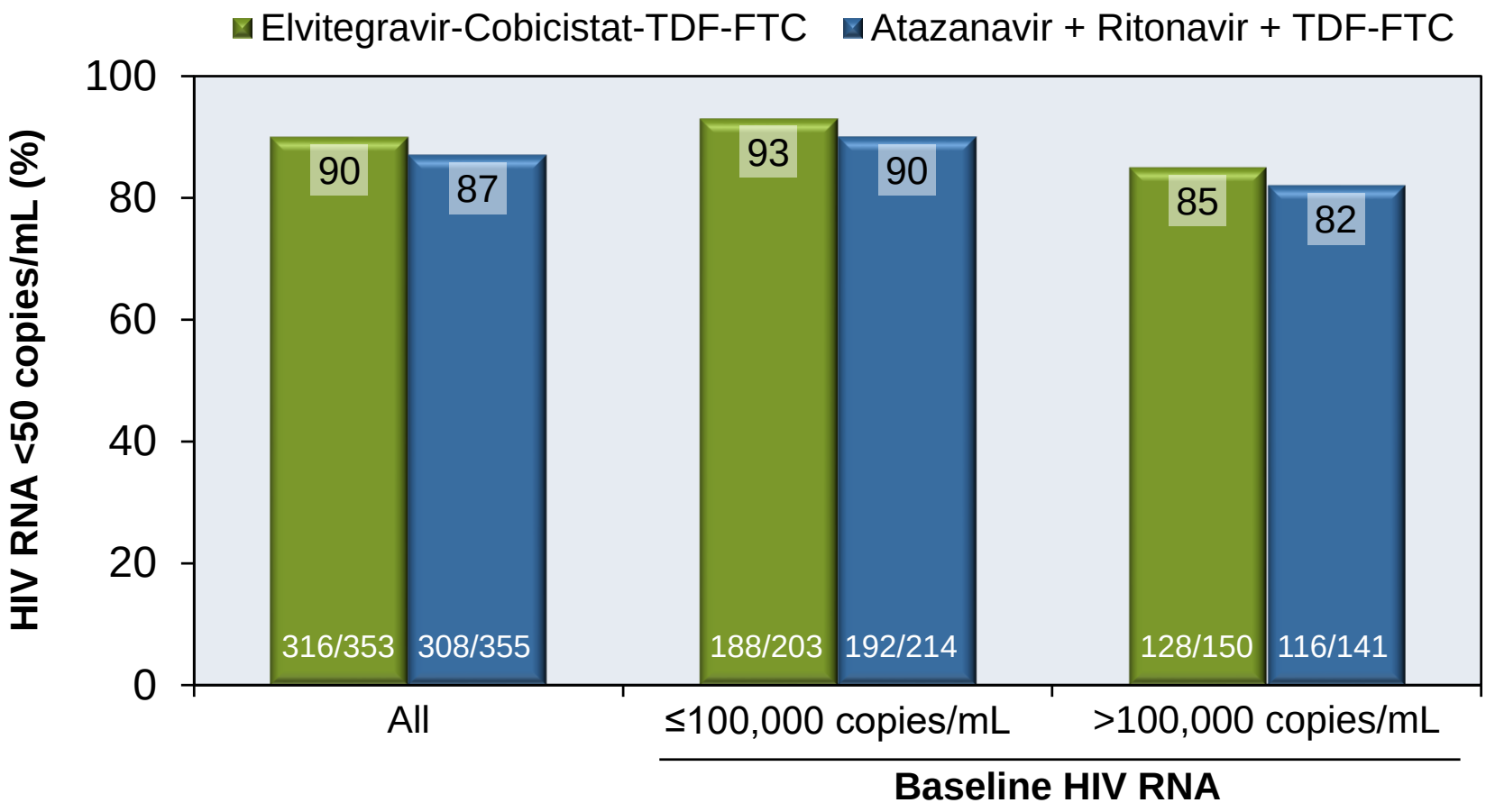
- **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir-emtricitabine with atazanavir + ritonavir + tenofovir DF-emtricitabine
- **Inclusion Criteria (n = 708)**
  - Antiretroviral-naïve adults
  - Age ≥18
  - HIV RNA ≥5,000 copies/ml
  - Any CD4 count
- **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: Result

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




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

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# 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.**

# 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 Study: Design

## Study Design: 104/111

- **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine with elvitegravir-cobicistat-tenofovir DF-emtricitabine
- **Inclusion Criteria (n = 1733)**
  - Antiretroviral-naïve adults
  - Age ≥18 years
  - 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

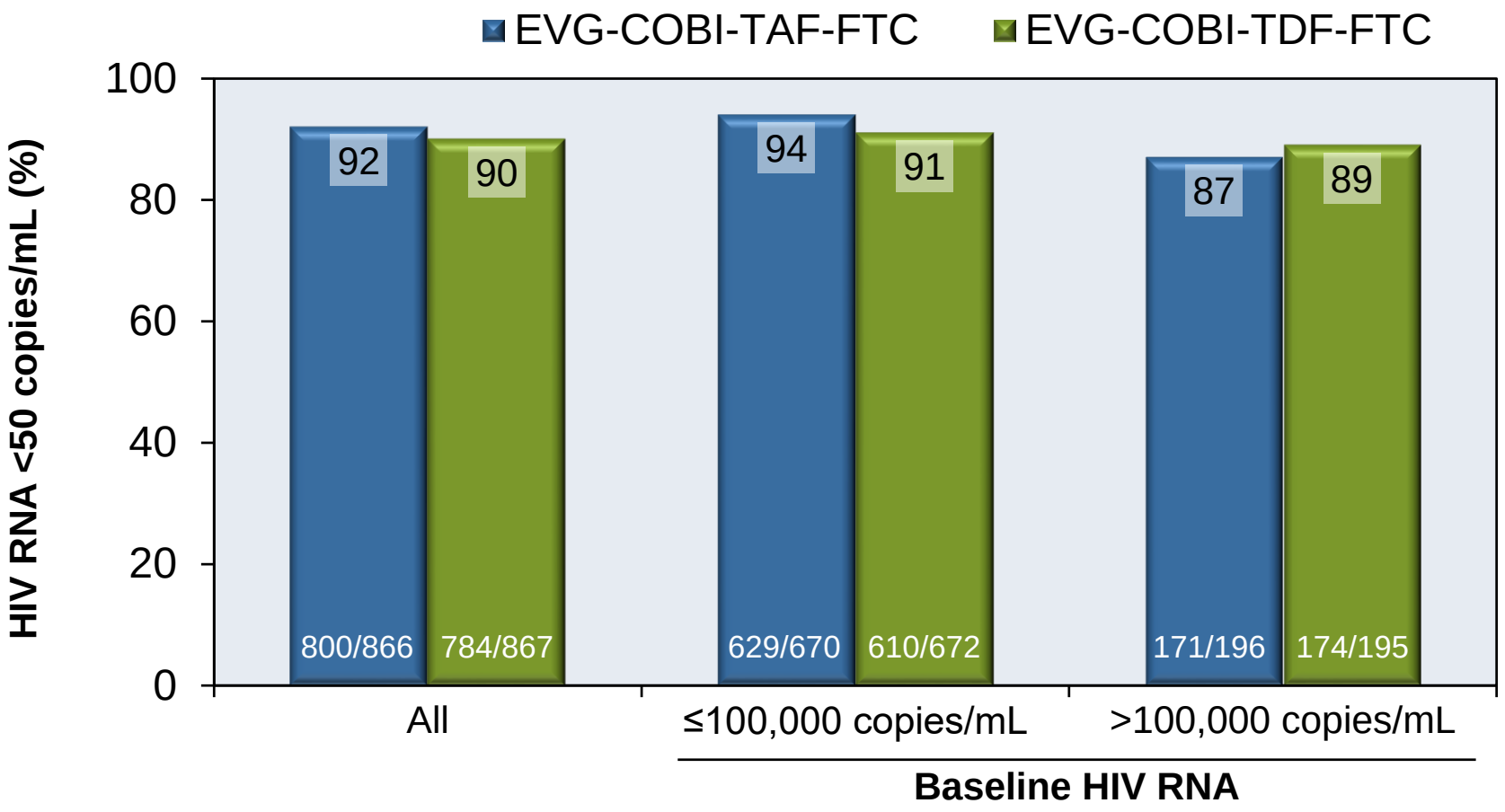
**EVG-COBI-TAF-FTC**
(*Genvoya*)
(n = 866)

**EVG-COBI-TDF-FTC**
(*Stribild*)
(n = 867)

**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.**

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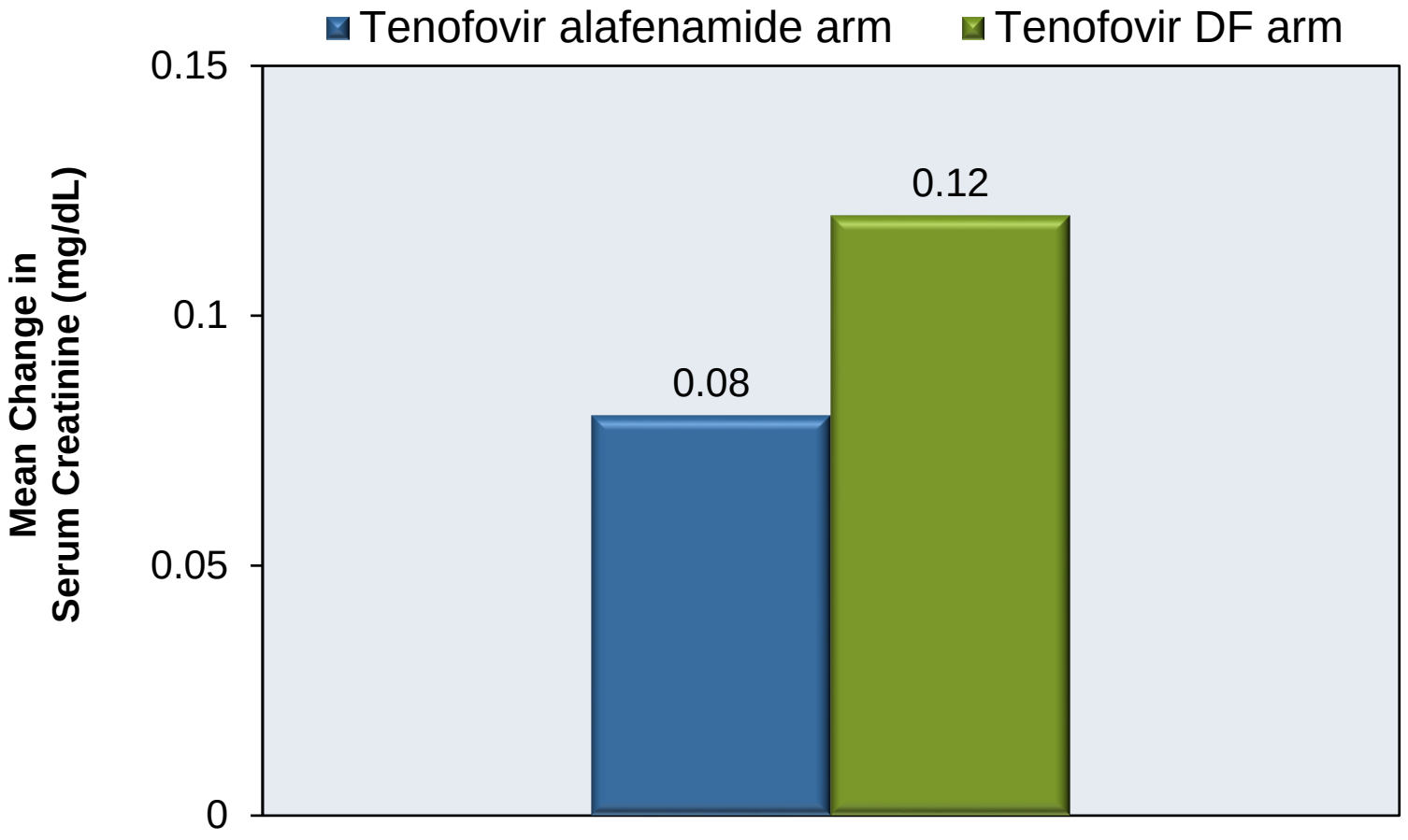
# EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
# Study 104/111: Adverse Effects

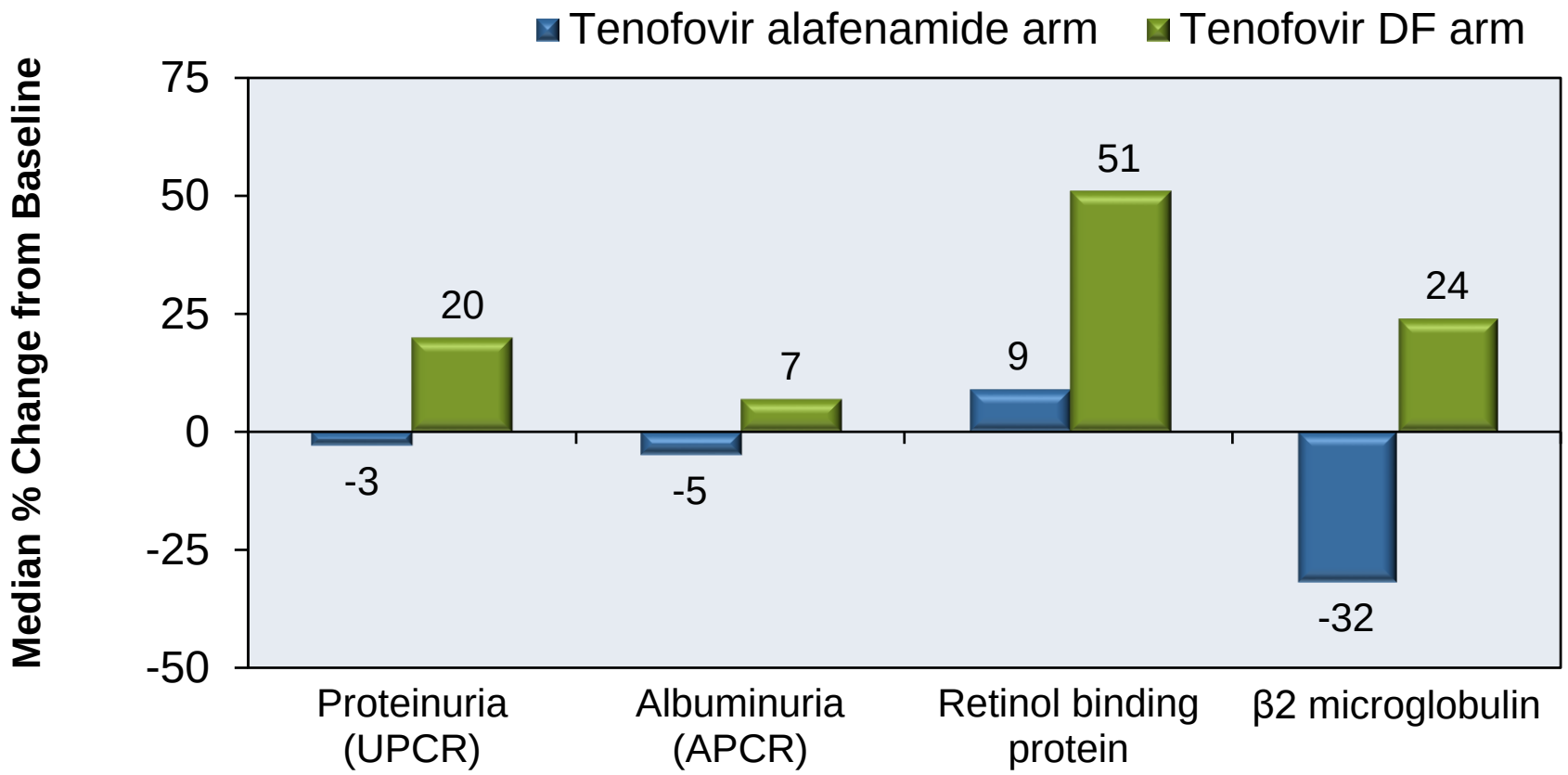
## Week 48: Change in Serum Creatinine from Baseline




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

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

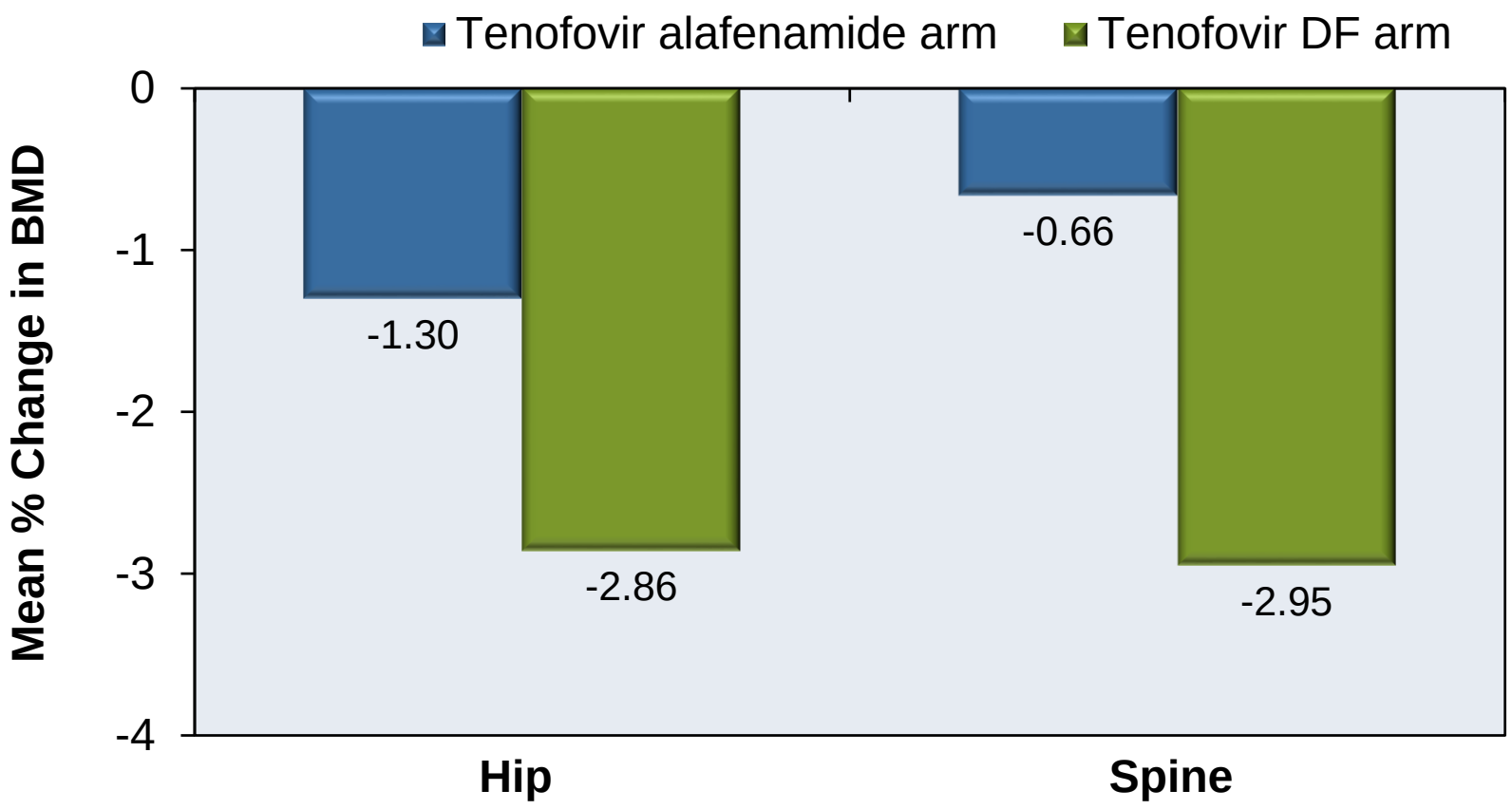
## Week 48: Changes in Quantitative Proteinuria




**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




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.**

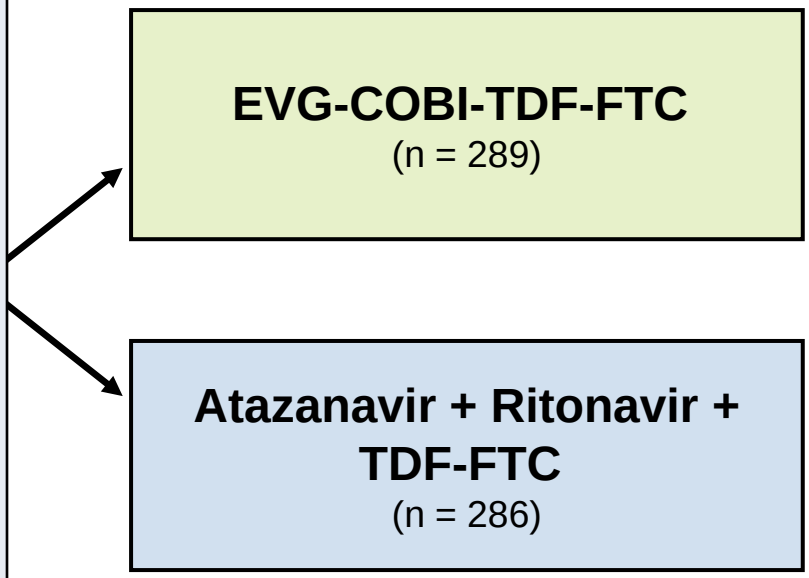
EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC in Women

# Study 128 (WAVES)

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

## Study Design: WAVES

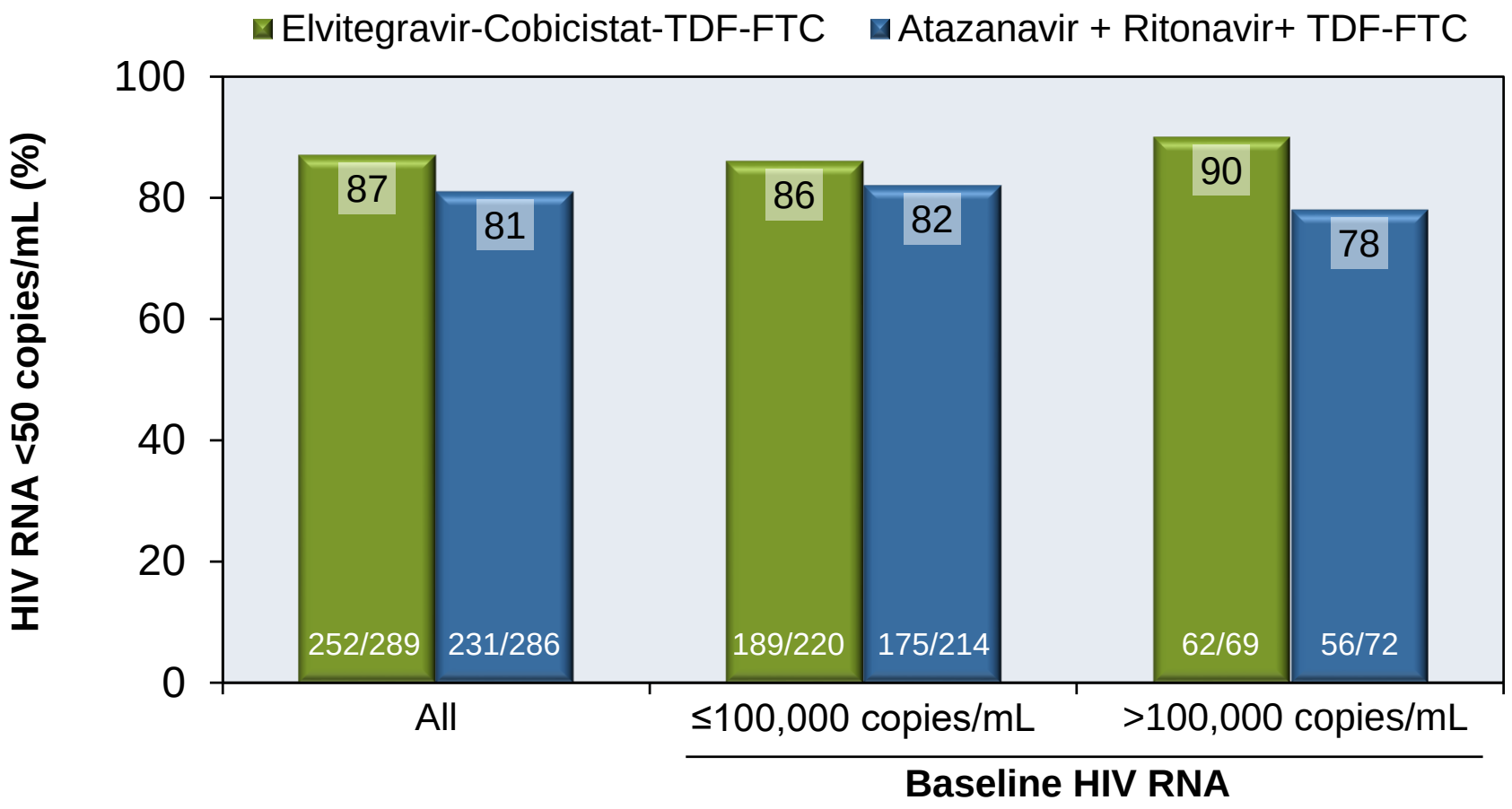
- **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir-emtricitabine with atazanavir + ritonavir + tenofovir DF-emtricitabine in women
- **Inclusion Criteria (n = 575)**
  - Antiretroviral-naïve women
  - Age ≥18 years
  - HIV RNA ≥500 copies/mL
  - Any 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: Snapshot Analysis (ITT, Missing=Failure)




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

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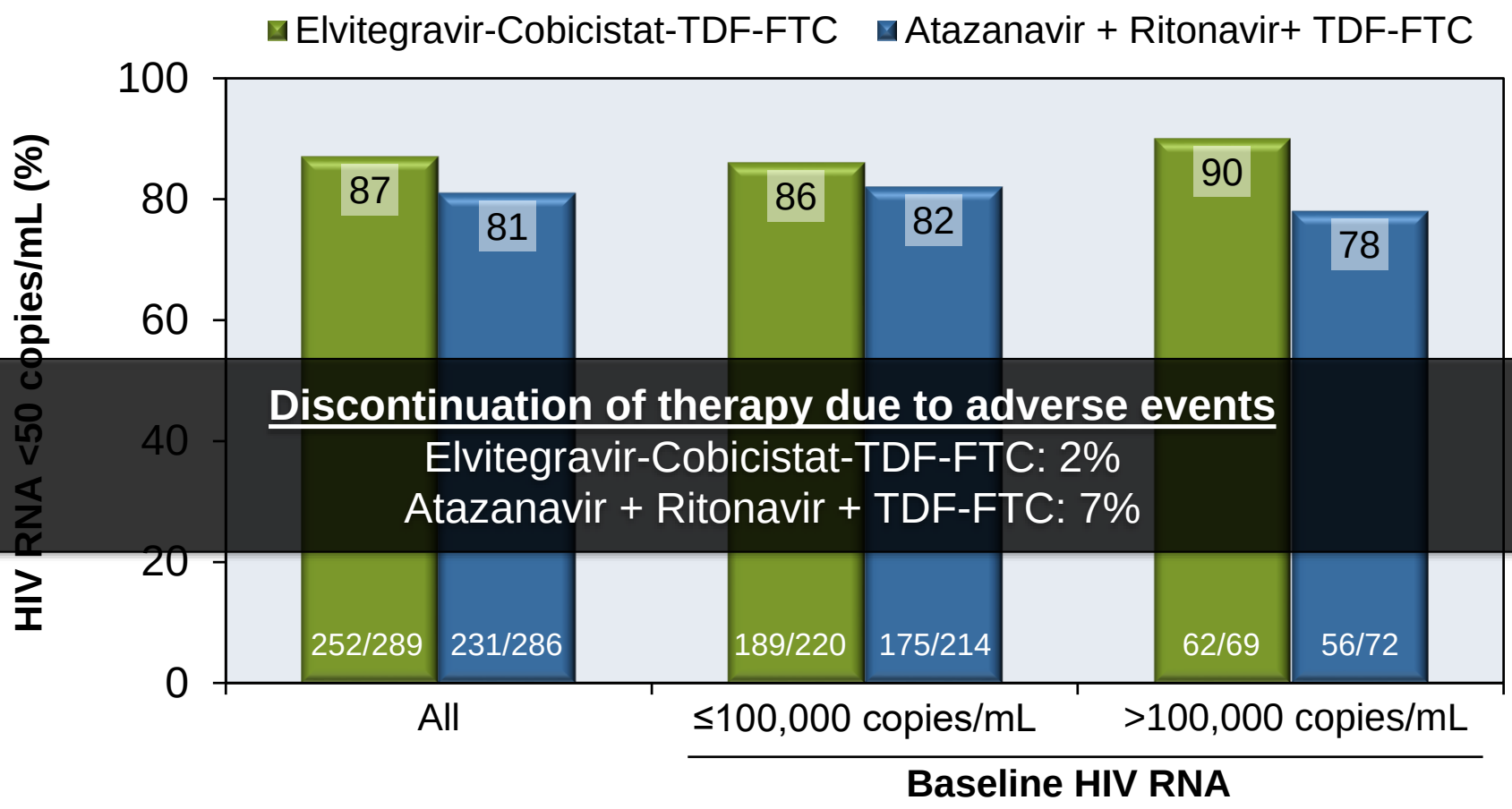
# EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC (in Women)
# WAVES Study: Result

## Week 48 Virologic Response: Snapshot Analysis (ITT, Missing=Failure)




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

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# 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.**

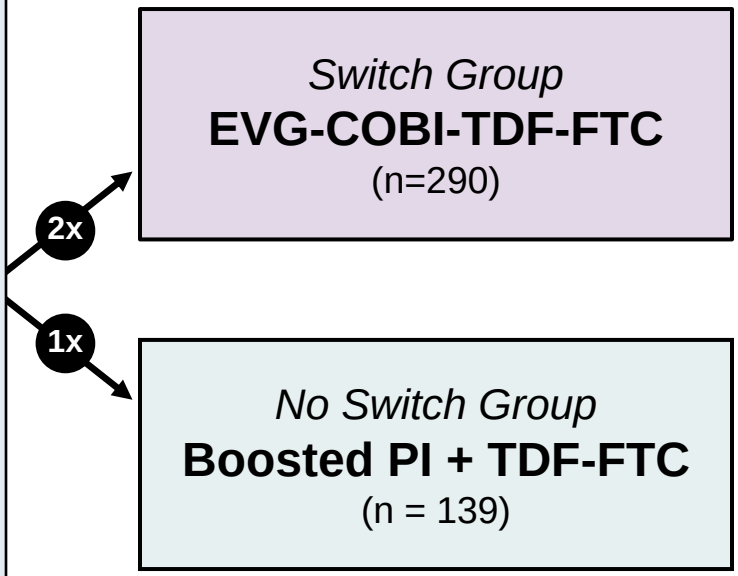
Switch from PI-Based Regimen to EVG-COBI-TDF-FTC

# Study 115 (STRATEGY-PI)

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

## Study Design: STRATEGY-PI

- **Background**: Open-label, randomized study, 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)

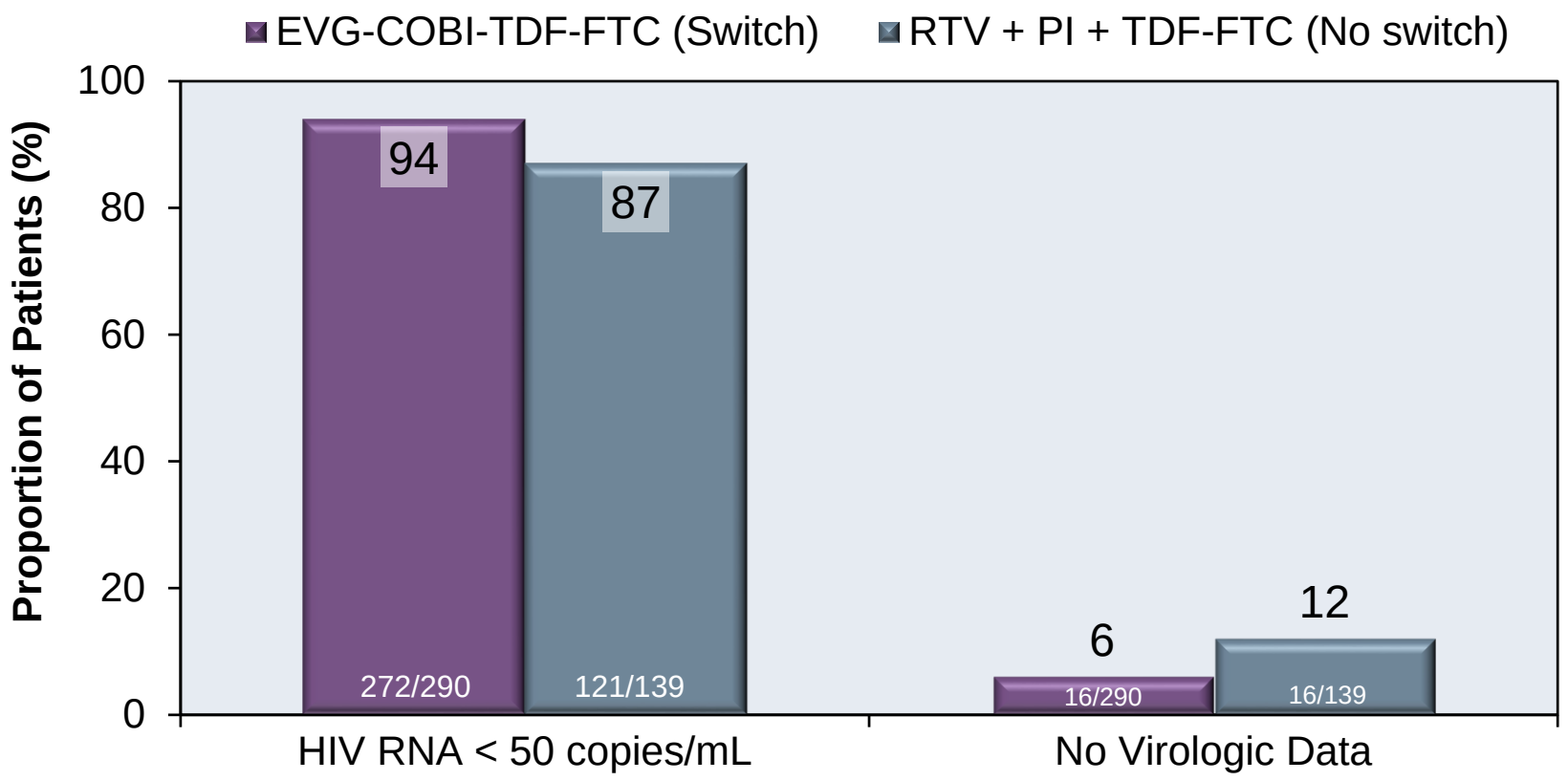



*__NOTE__: 3 participants from switch group, and 1 participant from no-switch group, were excluded from study after screening for protocol violations.

**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 (Modified Intent-to-Treat Analysis)




**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 supressed adults with HIV taking a multitablet ritonavir-boosted protease inhibitor regimen.”

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

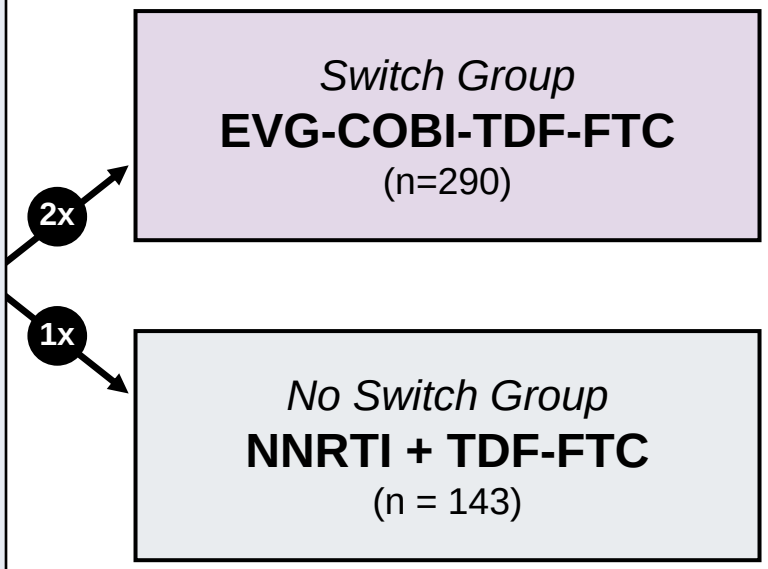
Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC

# Study 121 (STRATEGY-NNRTI)

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

## Study Design: STRATEGY-NNRTI

- **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 or
  - CrCl ≥70 mL/min
- **Treatment Arms**
  - EVG-COBI-FTC-TDF (Switch group)
  - Remain on NNRTI + FTC-TDF (No switch group)

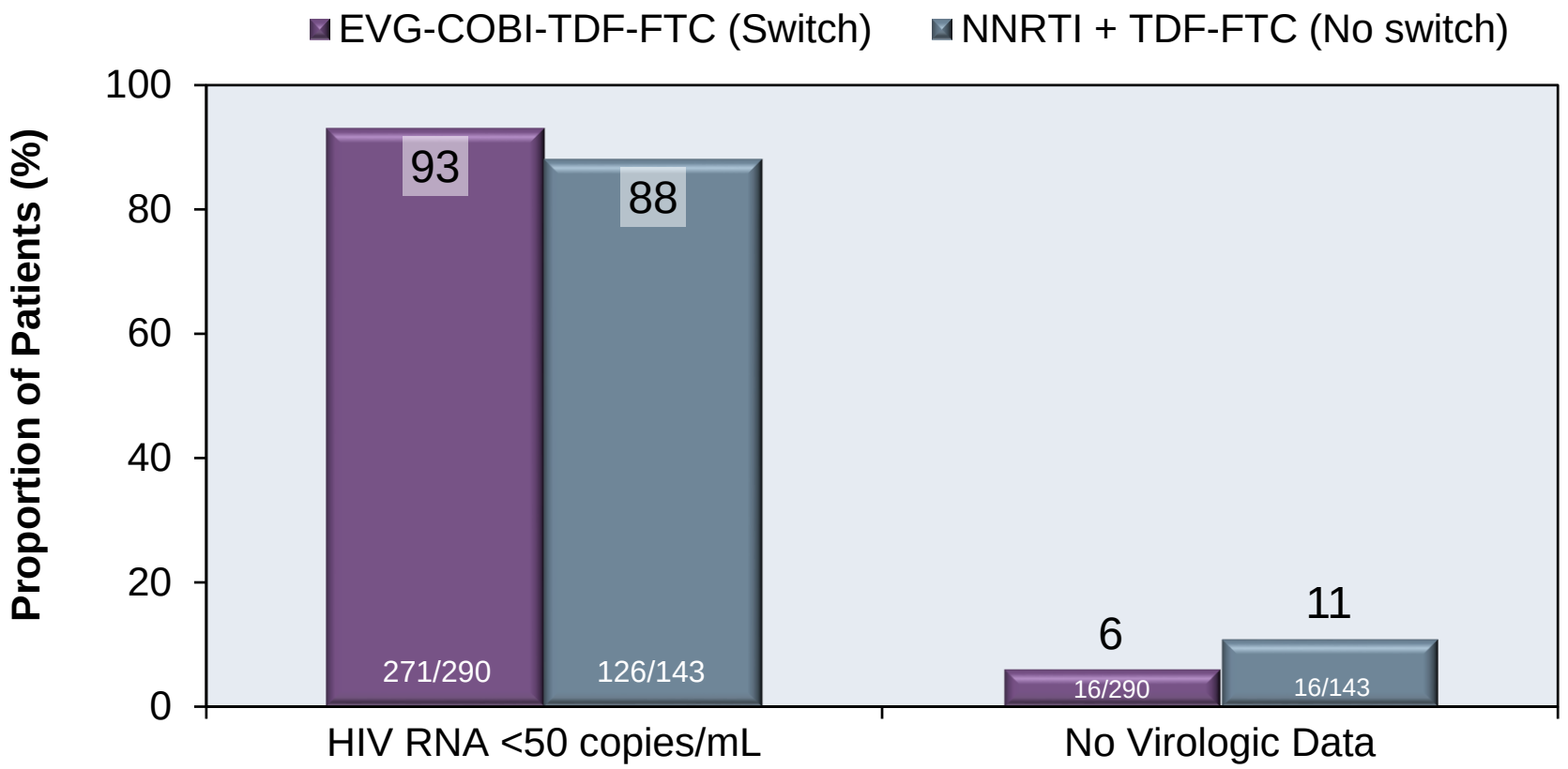



*__NOTE__: 2 participants from switch group and 4 participants from no-switch group were excluded from the study after screening (2 protocol violation,1 non-adherence, 3 withdrew consent)

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

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

## Week 48: Virologic Response (Modified Intent-to-Treat Analysis)




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

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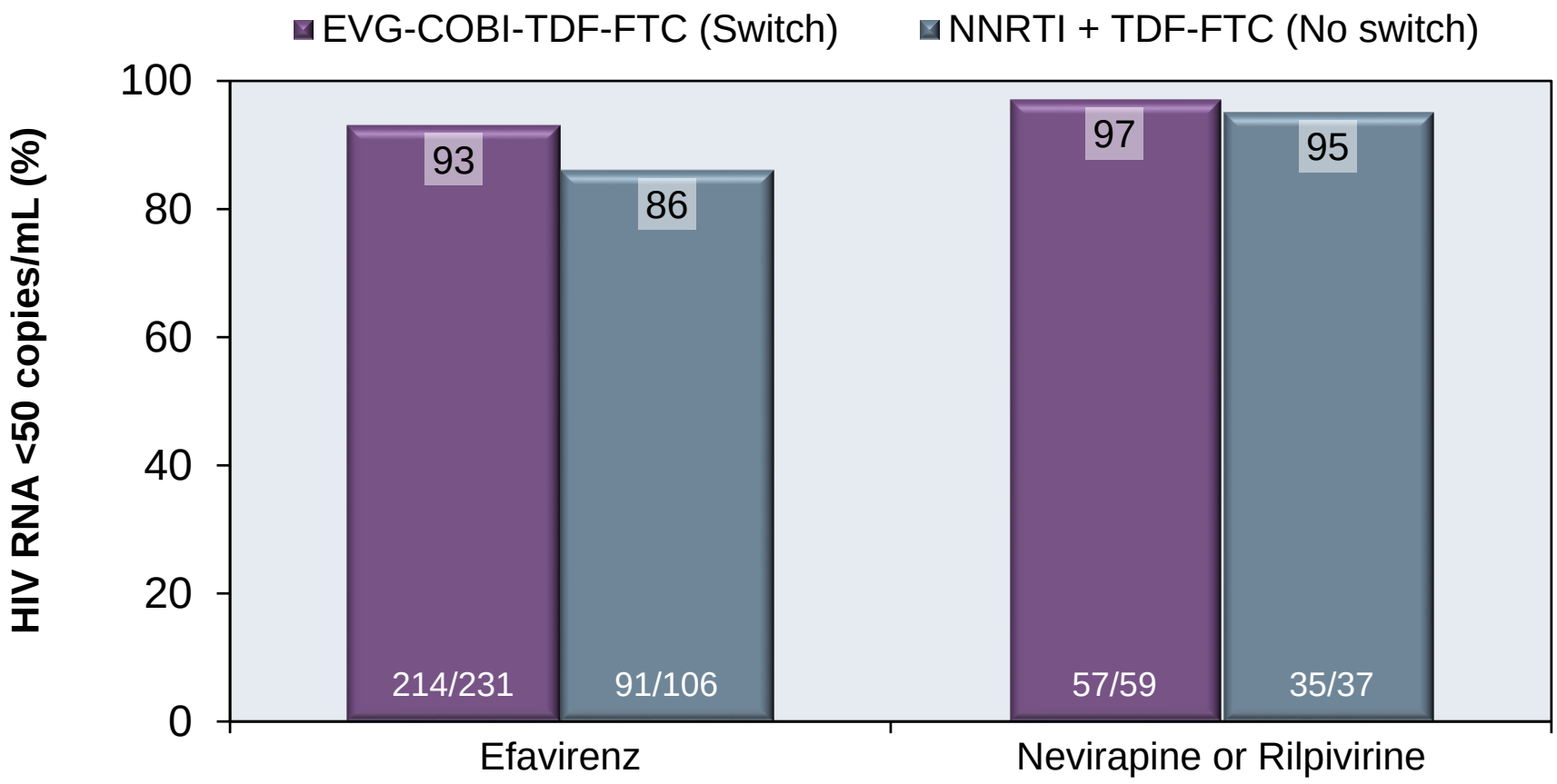
# Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC
# STRATEGY-NNRTI: Subgroup Analysis Result

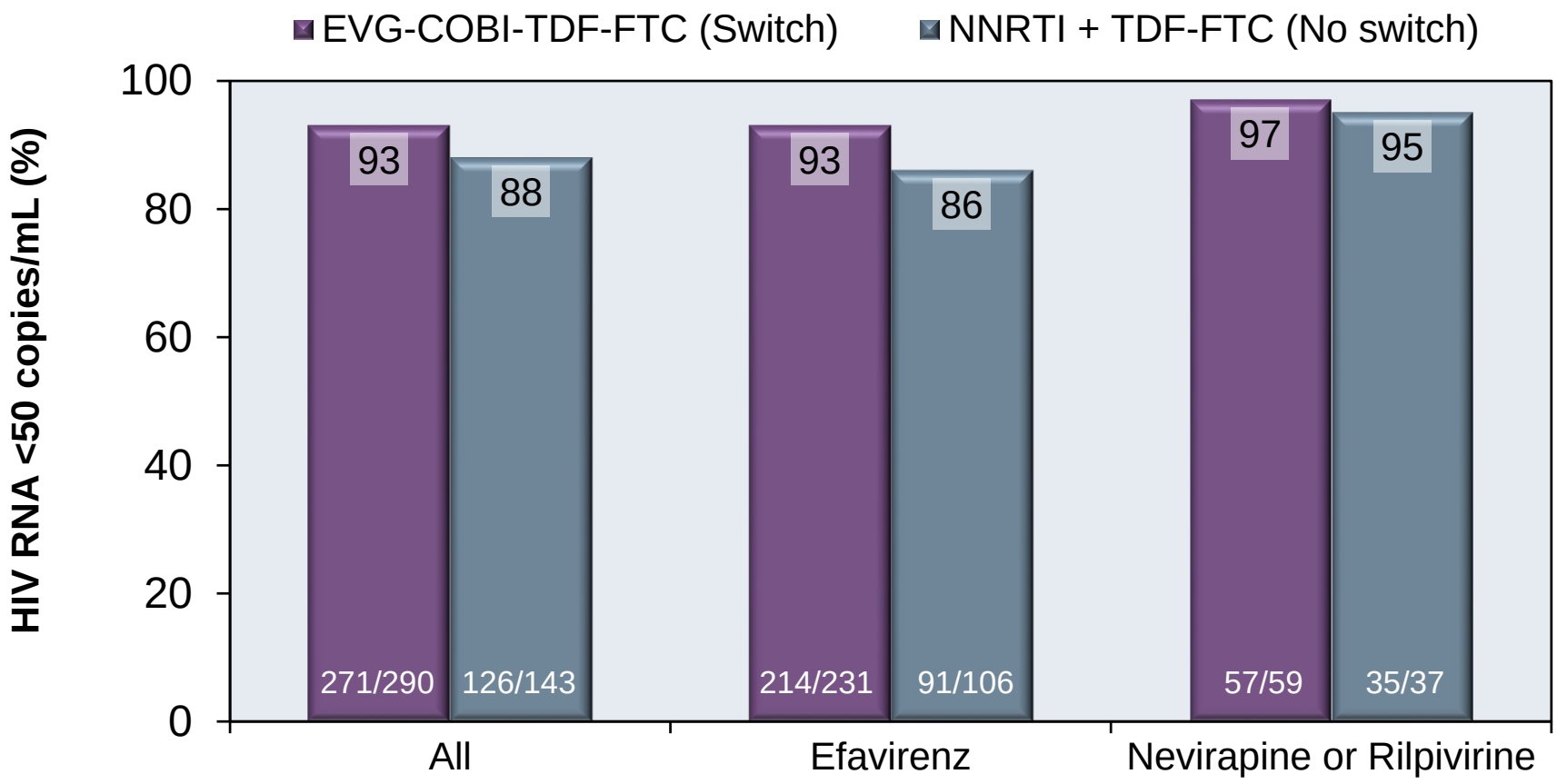
## Week 48 Virologic Response, by Baseline NNRTI Regimen




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

# Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC
# STRATEGY-NNRTI: Subgroup Analysis Result

## Week 48 Virologic Response, 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: Study 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.**

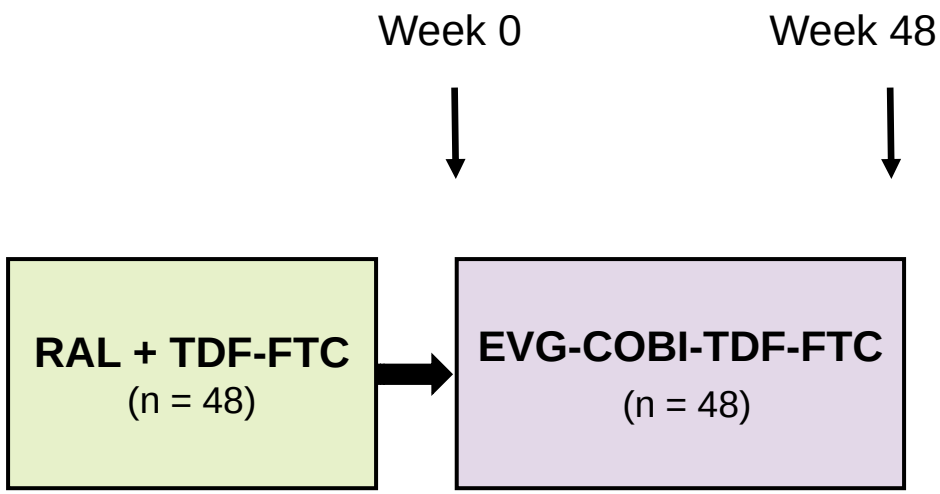
Switch to Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

# Study 123

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

**Study Design: 123**

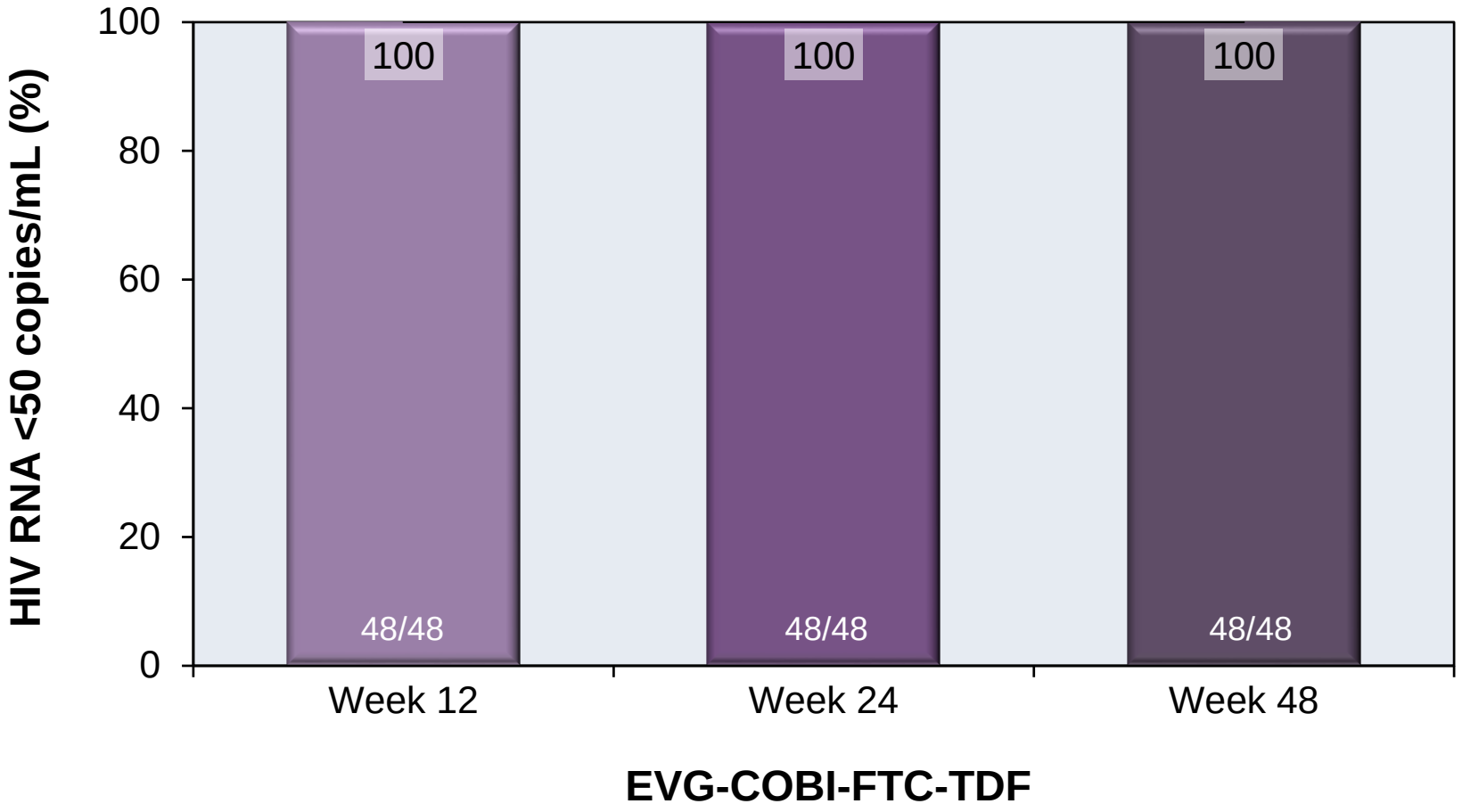
- **Background**: Open-label, randomized study, Phase 3b trial evaluating switching to once-daily elvitegravir-cobicistat-tenofovir DF-emtricitabine from twice daily raltegravir plus tenofovir DF-emtricitabine
- **Inclusion Criteria (n = 48)**
  - HIV RNA <50 copies/mL
  - On RAL+ TDF-FTC for ≥6 months
  - 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: Design

## 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

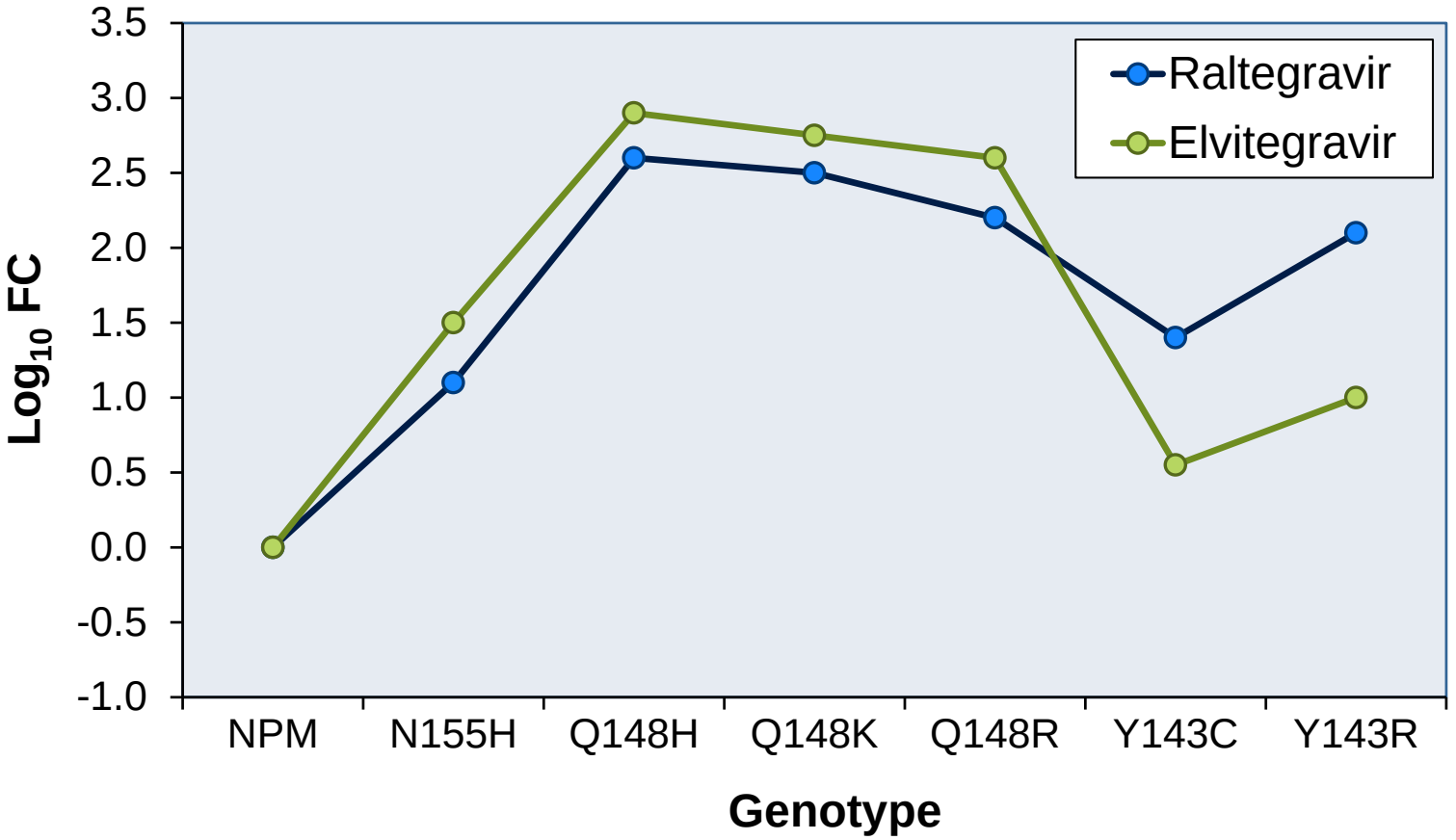
**Conclusion**: “All participants switching to 1 tablet once-a-day elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (*Stribild*) from a twice-daily raltegravir + emtricitabine/tenofovir disoproxil fumarate regimen remained virologically suppressed. *Stribild* was well tolerated. Switching 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.**

# Elvitegravir Resistance

# Raltegravir and Elvitegravir: Cross Resistance

Graphical Representation of Mean log10 Fold Change Values for Different Genotype




NPM = no primary mutation

**Source: Van Wesenbeek L, et al. Antimicrob Agents Chemo. 2011:55:321-5.**

# Resistance Data with EVG-Cobi-TDF-FTC Virologic Failures
## Data from Studies 102 and 103

| Resistance Data from Studies 102 and 103 | |
|---|---|
| **Subjects with Virologic Failure (N = 13)** | |
| **NRTI Resistance: Genotype Data** | **N = 12** |
| A62A/V | 2 (17%) |
| K65R | 4 (33%) |
| M184V | 12 (100%) |
| **ISTI Resistance Genotype Data: 1° Mutations** | **N = 11** |
| T66I | 2 (18%) |
| E92Q | 8 (73%) |
| Q148R | 3 (27%) |
| N155H | 3 (27%) |

**Source: White KL, et al. IWDR 2012: Abstract 4.**

## Resistance Data with EVG-Cobi-TDF-FTC Virologic Failures

# Genotypic Data from Studies 102 and 103

| Patient | Genotype Data from Patients with Virologic Failure (N = 13) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | NRTI | | | INSTI | | | | | | | | |
| | | | | Primary | | | | Secondary | | | | |
| 1 | A62V | K65R | M184V | | | Q148R | | | | G140C | | |
| 2 | A62V | K65R | M184V | | E92Q | | | H51Y | L68V | | | |
| 3 | | K65R | M184V | | E92Q | | | | | | S153A | |
| 4 | ND | | | T66A/I | E92Q | | N155H | | | | | E157Q |
| 5 | | | M184V | | E92Q | Q148R | N155H | | | | | |
| 6 | | | M184V | | E92Q | | | | | | | |
| 7 | | | M184V | | E92Q | | | | | | | |
| 8 | | | M184V | | | | N155H | | | | | |
| 9 | | | M184I | | E92Q | | | | | | | |
| 10 | | | M184V | | | Q148R | | | | | | |
| 11 | | | M184V | T66I | E92Q | | | | | | | |
| 12 | | K65R | M184V/I | | | | | | | | | |
| 13 | | | M184V | | | | | | | | | |

Most common pattern of resistance: M184V and E92Q

**Source: White KL, et al. IWHHVDR 2012: Abstract 4.**

## Resistance Data with EVG-Cobi-TDF-FTC Virologic Failures

# Phenotypic Data from Studies 102 and 103

| Patient | Integrase Strand Transfer Inhibitor and Mean Fold Value Change | |
|---|---|---|
| | **Elvitegravir** (biologic cut-off = 2.5) | **Raltegravir** (biologic cut-off = 1.5) |
| 1 | >198 | 28 |
| 2 | 149 | 6.2 |
| 3 | 111 | 3.3 |
| 4 | 54 | 6.0 |
| 5 | 51 | 12 |
| 6 | 44 | 3.6 |
| 7 | 36 | 3.0 |
| 8 | 36 | 11 |
| 9 | 28 | 3.3 |
| 10 | 23 | 8.7 |
| 11 | 5.6 | 1.8 |

**Source: White KL, et al. IWHHVDR 2012: Abstract 4.**

# Integrase Strand Transfer Inhibitors
# Primary Resistance Associated Mutations (RAMs)

## Elvitegravir: Primary INSTI-Resistance Associated Mutations

| | T | E | T | S | Q | N | |
|---|---|---|---|---|---|---|---|
| **Elvitegravir** | **66** | **92** | **97*** | **147** | **148** | **155** | **IN** |
| | I<br>A<br>K | Q<br>G | A | G | R<br>H<br>K | H | |

## Raltegravir: Primary INSTI-Resistance Associated Mutations

| | E | T | Y | Q | N | |
|---|---|---|---|---|---|---|
| **Raltegravir** | **92** | **97*** | **143** | **148** | **155** | **IN** |
| | Q | A | R<br>H<br>C | R<br>H<br>K | H | |

*T97A may require additional mutations for resistance

**Source: Abram ME, et al. . IWHHVDR 2012: Abstract 3.**

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## Resistance Data with EVG-Cobi-TDF-FTC Virologic Failures

# Phenotypic Data from Studies 102 and 103

| Patient | Integrase Strand Transfer Inhibitor and Mean Fold Value Change | |
|---|---|---|
| | **Elvitegravir** (biologic cut-off = 2.5) | **Raltegravir** (biologic cut-off = 1.5) |
| 1 | >198 | 28 |
| 2 | 149 | 6.2 |
| 3 | 111 | 3.3 |
| 4 | 54 | 6.0 |
| 5 | 51 | 12 |
| 6 | 44 | 3.6 |
| 7 | 36 | 3.0 |
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| 9 | 28 | 3.3 |
| 10 | 23 | 8.7 |
| 11 | 5.6 | 1.8 |

**Source: White KL, et al. IWHHVDR 2012: Abstract 4.**

# Acknowledgment

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