National HIV Curriculum

Etravirine (*Intelence*)

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AETC AIDS Education & Training Center Program

Etravirine (*Intelence*)

Intelence

[in-tel-ence]

100 mg 200 mg

NNRTI

Dose: 200 mg twice daily following a meal

Etravirine (*Intelence*)

- **Class**
  - non-nucleoside reverse transcriptase inhibitor
- **Approval**
  - FDA-approved January 22, 2008
- **Indication**
  - Combined with other ARVs for treatment-experienced adults
- **FDA-Approved Dose**
  - 200 mg twice daily following a meal
- **Metabolism**
  - Primarily in liver via cytochrome P450 enzymes
- **Adverse Events**
  - Nausea, rash, peripheral neuropathy

Etravirine
Summary of Key Studies

- Phase 3 Trials in Treatment Naïve
  - SENSE: Etravirine once daily versus Efavirenz
  - 08-2070: Etravirine once daily
- Phase 3 Trials in Treatment Experienced
  - DUET-1: Etravirine + Darunavir + OBT
  - DUET-2: Etravirine + Darunavir + OBT
  - TRIO: Etravirine + Darunavir/r + Raltegravir + OBT

Etravirine
Summary of Key Studies

- Phase 2 Trials in Treatment Experienced
  - C223: Etravirine versus Placebo in highly resistant
  - C227: Etravirine versus PI in salvage
  - PIANO: Etravirine in adolescents and children
- Simplification and Switch Studies
  - INROADS: Etravirine and Darunavir/r
  - ETRA-SWITCH: Switch from PI to Etravirine
  - SWITCH-EE: Switch from Efavirenz to Etravirine
  - SSAT-029: Switch from Efavirenz to Etravirine

INITIAL THERAPY

Etravirine

Once Daily Etravirine versus Efavirenz in Treatment-Naive

SENSE Trial

Once Daily Etravirine *versus* Efavirenz in Treatment-Naive SENSE: Study Design

Study Design: SENSE Study

- **Background**: Randomized, controlled, double-blind, phase 2 trial evaluating efficacy of once-daily etravirine compared with efavirenz in treatment-naïve persons with HIV
- **Inclusion Criteria (n = 157)**
  - Age ≥18 years
  - Antiretroviral-naïve
  - HIV RNA >5000 copies/mL
  - No resistance to study drugs
- **Treatment Arms**
  - ETR 400 mg daily + 2NRTIs*
  - Efavirenz 600 mg daily + 2NRTIs*

*NRTIs = tenofovir DF-emtricitabine, abacavir, lamivudine, or zidovudine-lamivudine

Etravirine 400 mg once daily + 2 NRTIs
(n = 79)

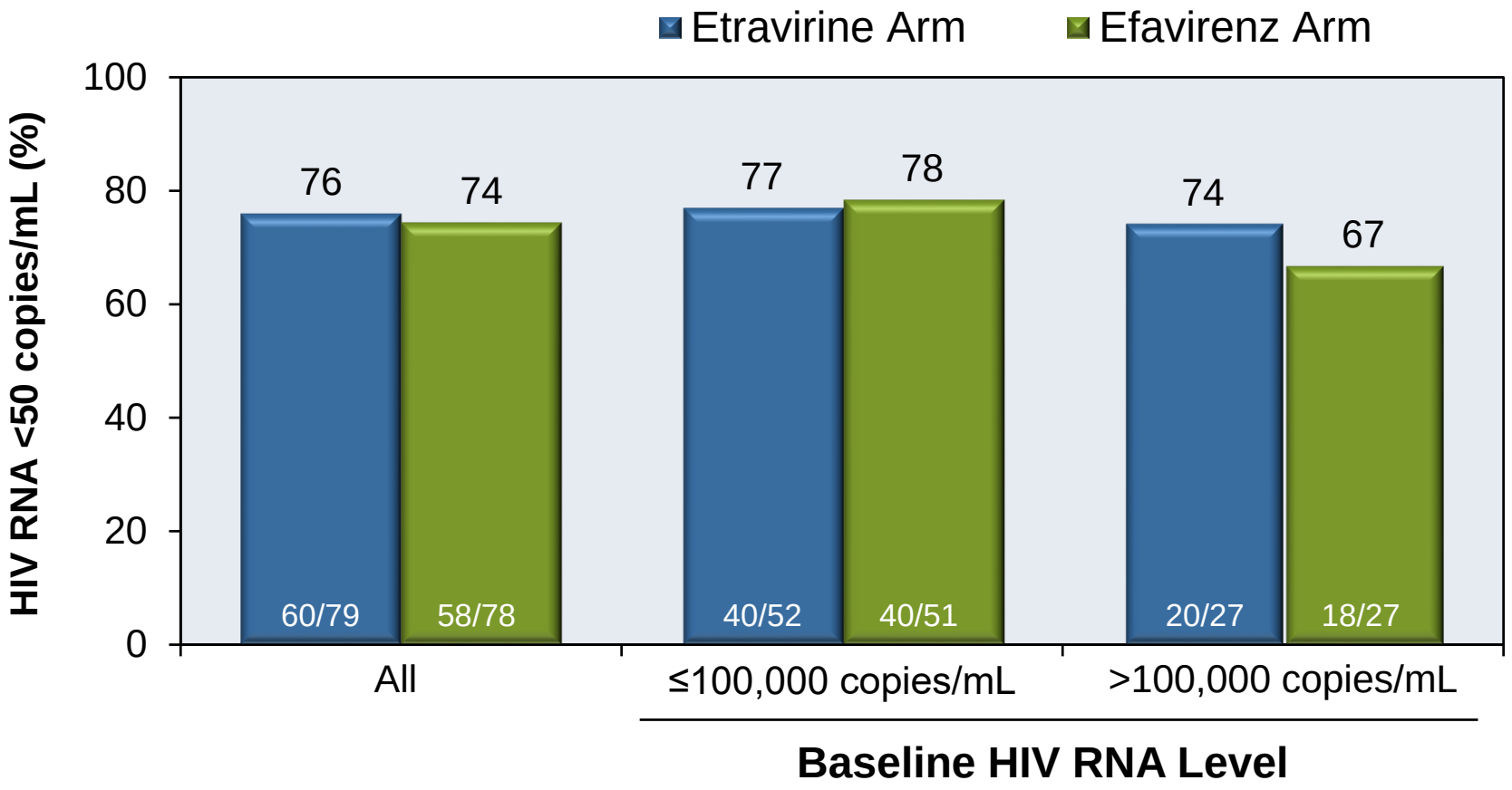
Efavirenz 600 mg once daily + 2 NRTIs
(n = 78)

SENSE = **S**tudy of **E**favirenz **N**europsychiatric events versu**S** **E**travirine

Source: Gazzard B, et al. AIDS. 2011;25:2249-58.

Once Daily Etravirine *versus* Efavirenz
SENSE: Results

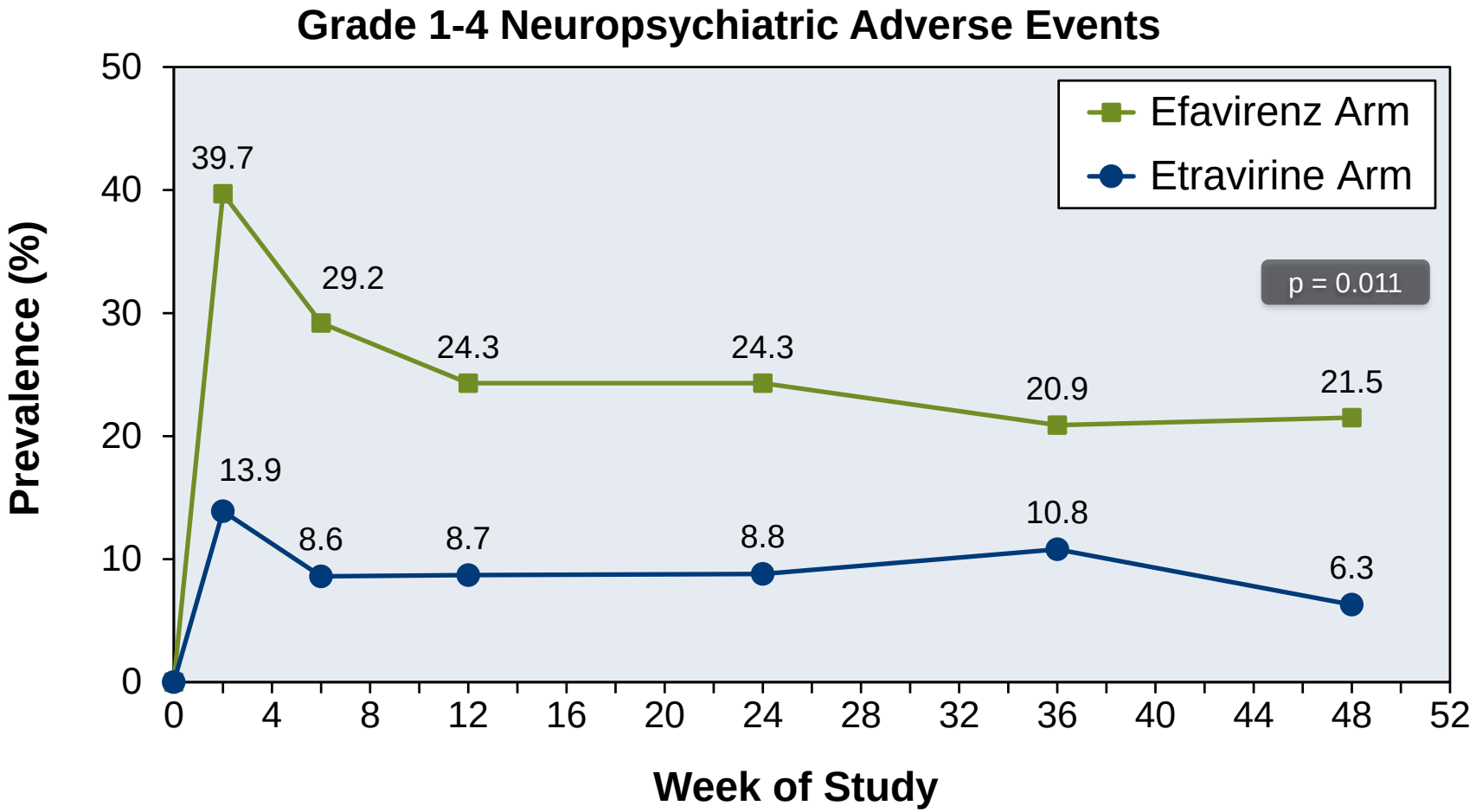
Week 48: Virologic Response (ITT-TLOVR*)



*ITT-TLOVR = Intention to Treat-Time to Loss of Virologic Response

Source: Gazzard B, et al. AIDS. 2011;25:2249-58.

Once Daily Etravirine *versus* Efavirenz
SENSE: Result



Source: Gazzard B, et al. AIDS. 2011;25:2249-58.

Once Daily Etravirine *versus* Efavirenz
SENSE: Conclusions

Conclusion: “First-line treatment with etravirine 400 mg once daily and two nucleoside reverse transcriptase inhibitors (NRTIs) led to similar rates of HIV RNA suppression, compared with efavirenz and two NRTIs. None of the patients with virological failure in the etravirine arm developed resistance to nonnucleosides.”

Source: Gazzard B, et al. AIDS. 2011;25:2249-58.

Once Daily Etravirine in Treatment-Naïve Adults
08-2070 Trial

Once Daily Etravirine in Treatment-Naïve Adults
08-2070: Design

Study Design: 08-2070

- **Background**: Phase 2, single-arm trial assessing activity, safety, and tolerability of once-daily etravirine with tenofovir DF-emtricitabine in treatment-naïve adults with HIV
- **Inclusion Criteria (n = 79)**
  - Age ≥18 years
  - HIV RNA >1000 copies/mL
  - Treatment-naïve
  - No resistance to etravirine or TDF-FTC
- **Treatment Arms**
  - Etravirine 400 mg QD + tenofovir-emtricitabine QD

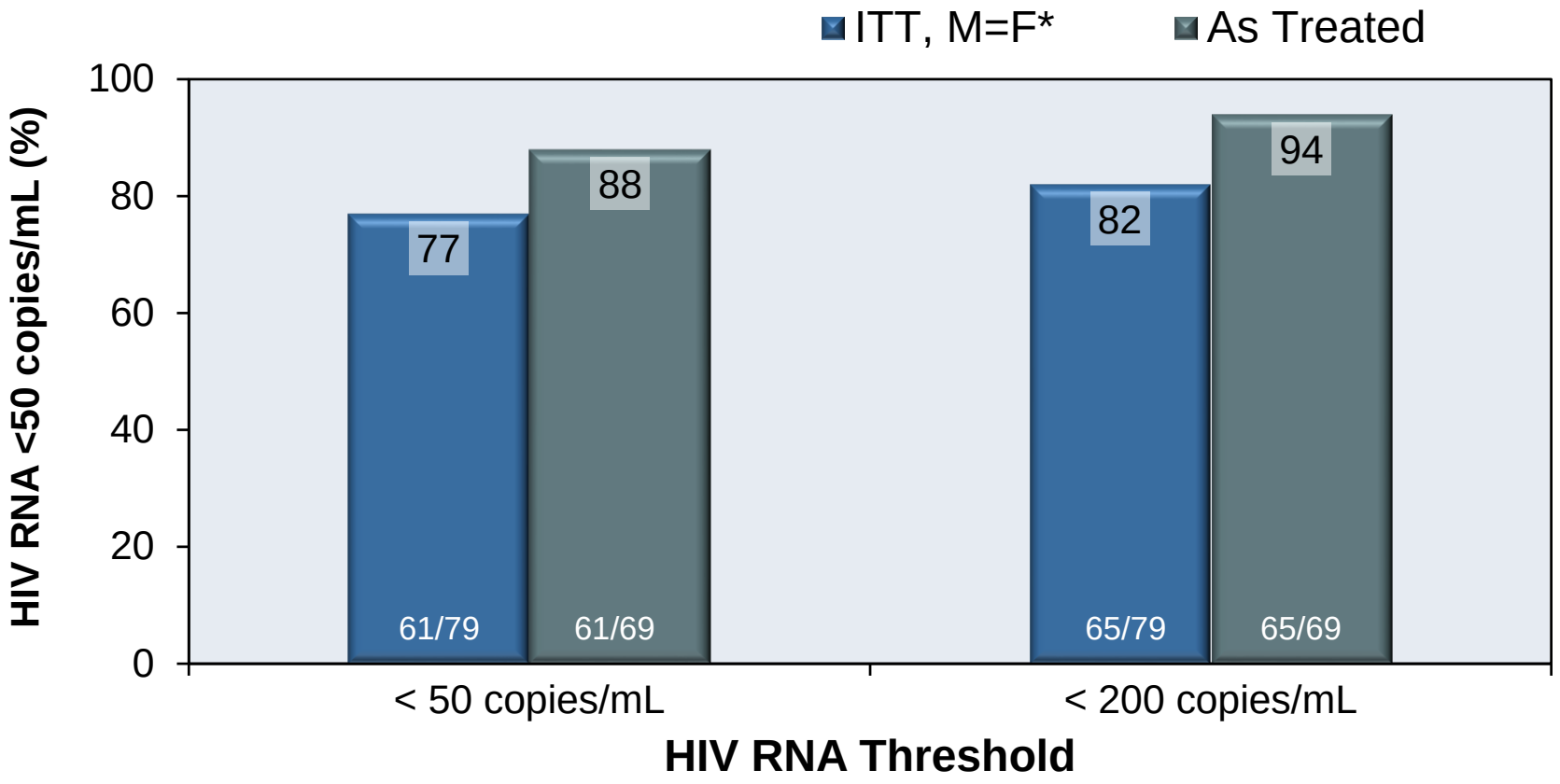
→ **Etravirine QD + Tenofovir-emtricitabine QD** (n = 79)

*ITT: Intent-to-Treat, M=F: missing equals failure

Source: Floris-Moore MA, et al. Antivir Ther. 2016;21:55-64.

Once Daily Etravirine in Treatment-Naïve Adults
08-2070: Result

Week 48: Virologic Response (all patients taking ETR + TDF-FTC)



*ITT: Intent-to-Treat, M=F: missing equals failure

Source: Floris-Moore MA, et al. Antivir Ther. 2016;21:55-64.

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Once Daily Etravirine in Treatment-Naïve Adults
08-2070: Result

Clinical Adverse Events and Laboratory Abnormalities through Week 48	
Variable	**Frequency (%)**
Rash (any grade)	5 (6.3)
Any grade 2 or higher event	18 (22.8)
New/worsened grade 3 or 4 sign/symptom	10 (12.7)
AST or ALT elevation (Grade 2 or higher)	5 (6.3)
Grade 2 creatinine elevation	2 (2.5)
New/worsened grade 3 or 4 laboratory abnormality	6 (7.6)
Etravirine discontinued due to toxicity	3 (3.8)

Source: Floris-Moore MA, et al. Antivir Ther. 2016;21:55-64.

Once Daily Etravirine in Treatment-Naïve Adults
08-2070: Conclusions

Conclusions: “In this study of ARV-naive HIV-positive adults, once-daily ETR with TDF/FTC had acceptable antiviral activity and was well-tolerated. Once-daily ETR may be a plausible option as part of a combination ARV regimen for treatment-naive individuals.”

Source: Floris-Moore MA, et al. Antivir Ther. 2016;21:55-64.

TREATMENT EXPERIENCED

Etravirine

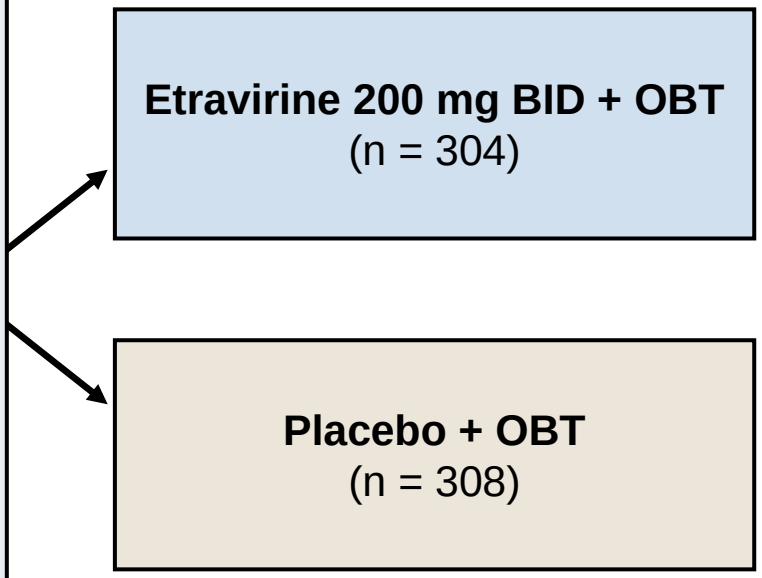
Etravirine in Treatment Experienced

DUET-1 (TMC125-C206)

Etravirine in Treatment Experienced
DUET-1: Study Design

Study Design: DUET-1

- **Background**: Randomized, controlled, double-blind, placebo-controlled phase 3 trial evaluating the long-term efficacy, tolerability, and safety of etravirine in treatment-experienced adults with HIV
- **Inclusion Criteria (n = 612)**
  - Age ≥18 years
  - On stable ARV regimen for ≥8 weeks
  - HIV RNA >5000 copies/mL
  - ≥3 primary PI mutations
  - ≥1 NNRTI resistance-associated mutation
- **Treatment Arms**
  - Etravirine 200 mg BID + OBT*
  - Placebo + OBT*

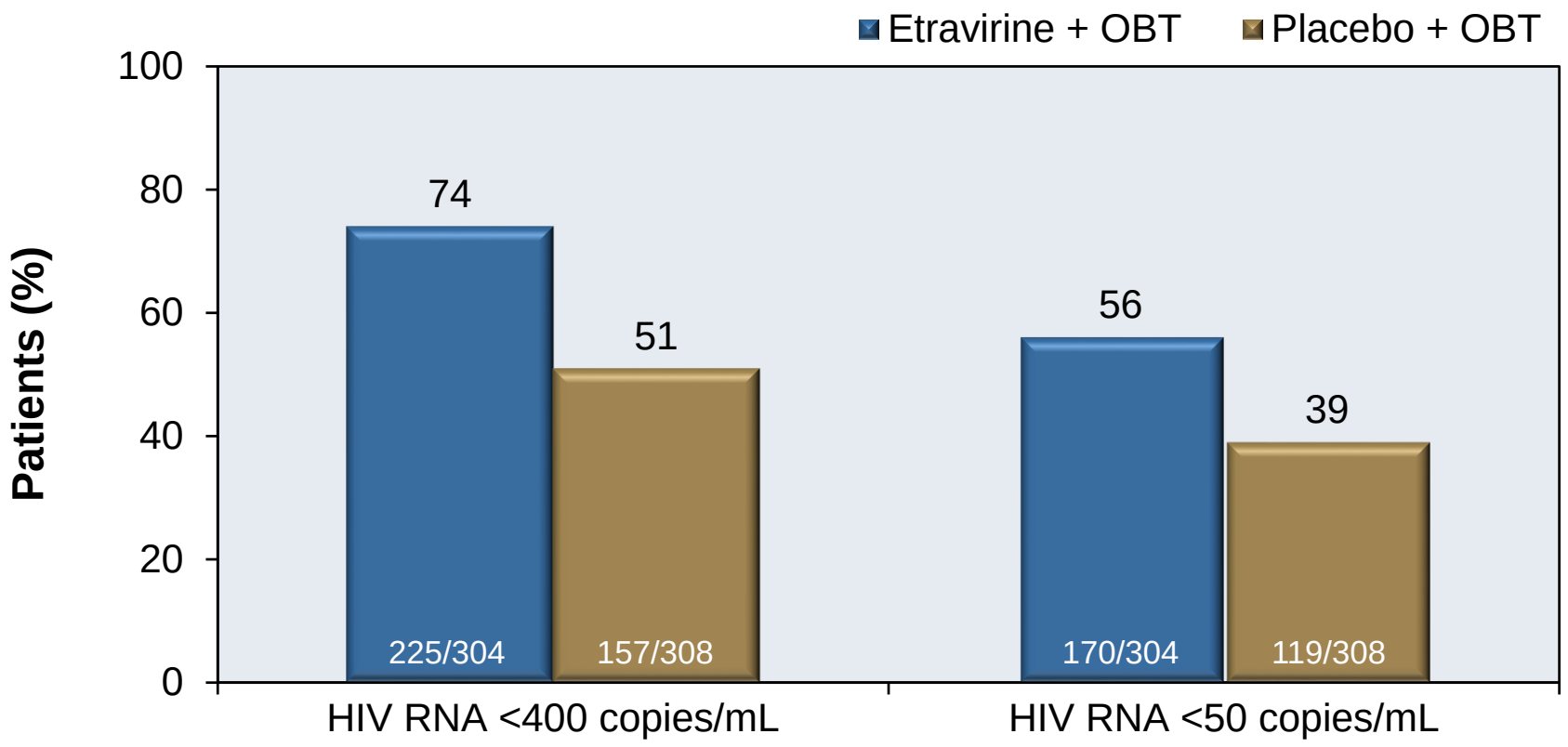


*OBT = NRTIs, Darunavir/r, +/- Enfuvirtide

Source: Madruga JV, et al. Lancet. 2007;370:29-38.

Etravirine in Treatment Experienced
DUET-1: Results

Week 24: Virologic Response (ITT-TLOVR*)



*ITT-TLOVR = Intention to Treat-Time to Loss of Virologic Response.

Source: Madruga JV, et al. Lancet. 2007;370:29-38.

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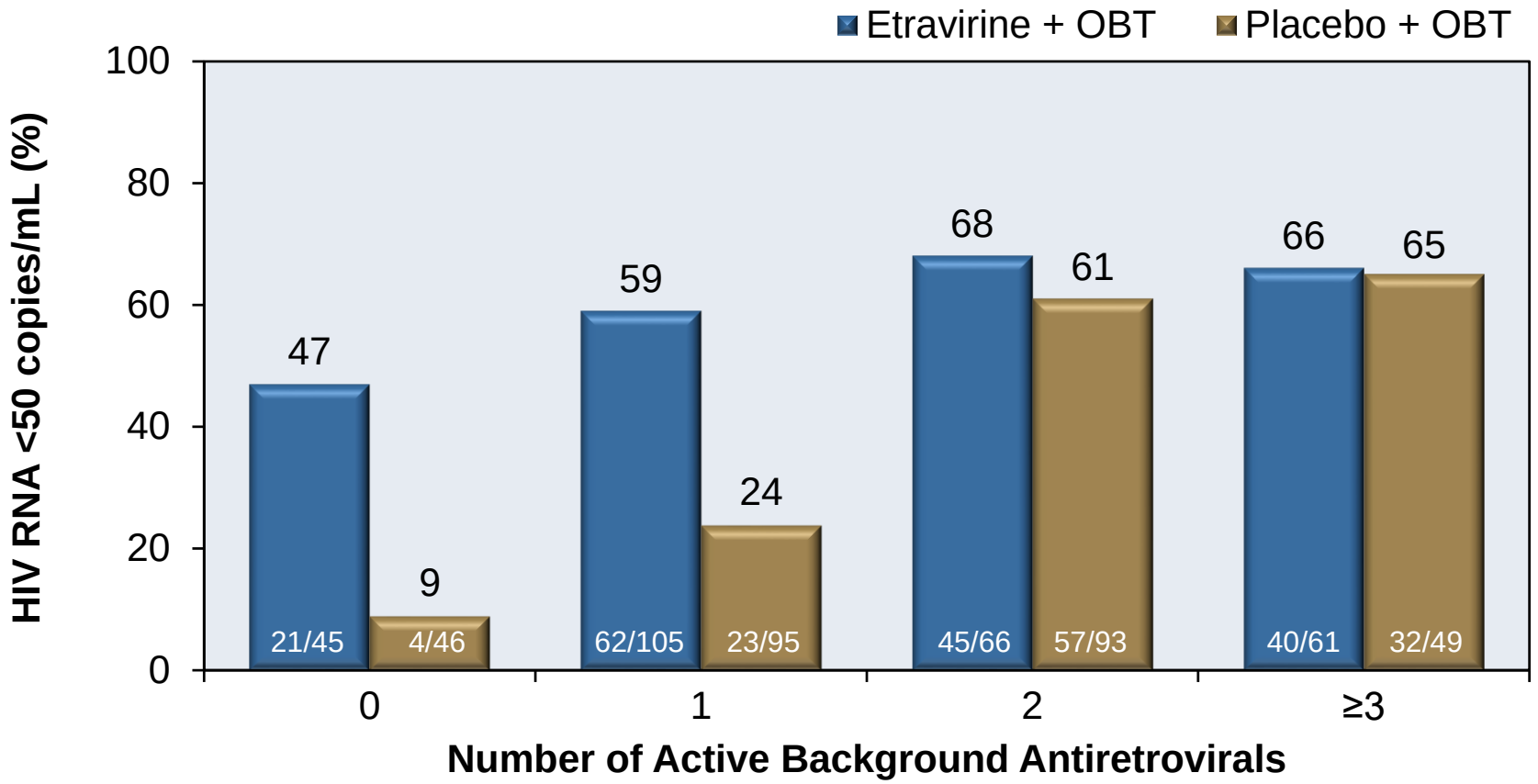
Etravirine in Treatment Experienced
DUET-2: Results

Week 24: Virologic Response (ITT-TLOVR*)

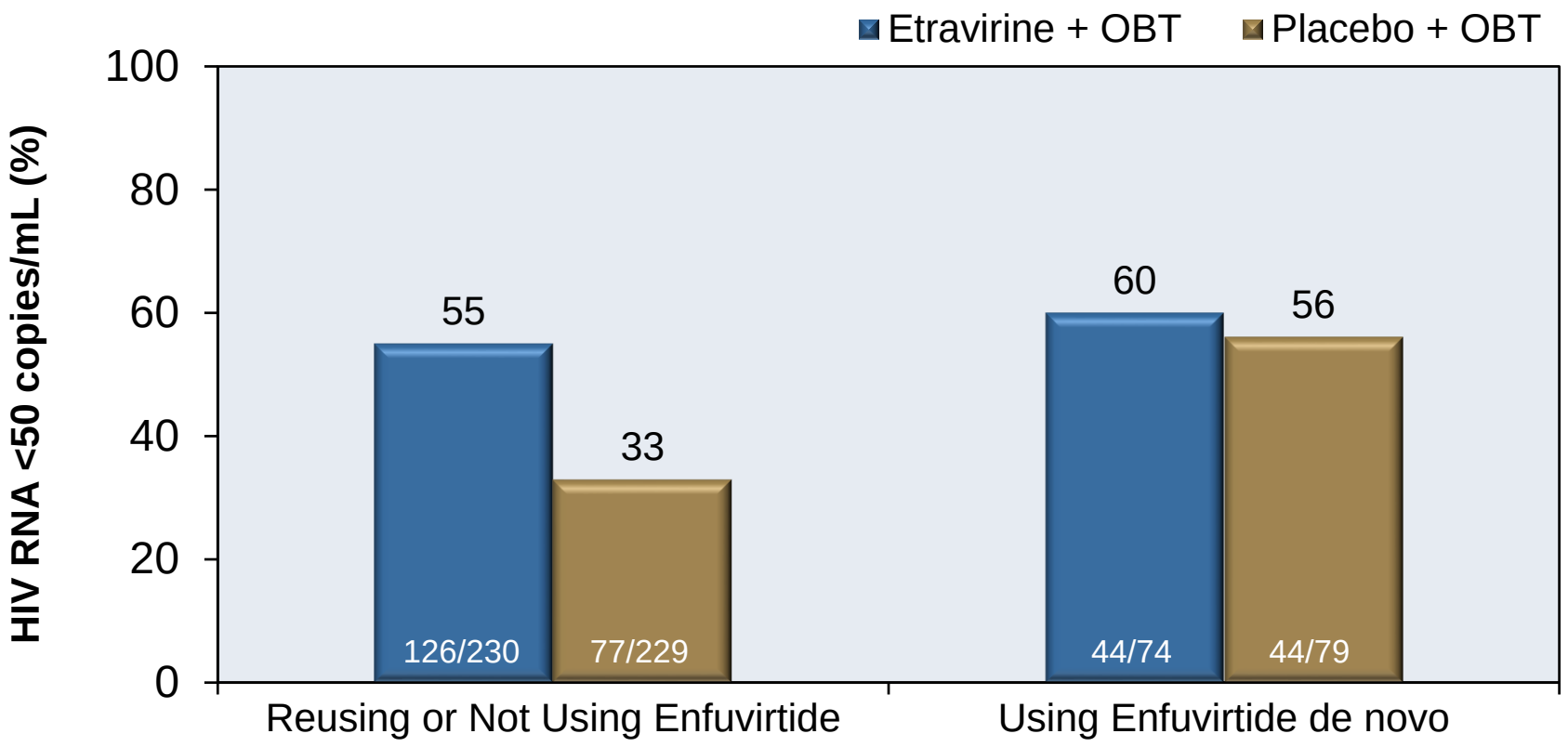


*ITT-TLOVR = Intention to Treat-Time to Loss of Virologic Response.

Source: Lazzarin A, et al. Lancet. 2007;370:39-48.

Etravirine in Treatment Experienced
DUET-1: Results

Week 24: Virologic Response (ITT-TLOVR*)

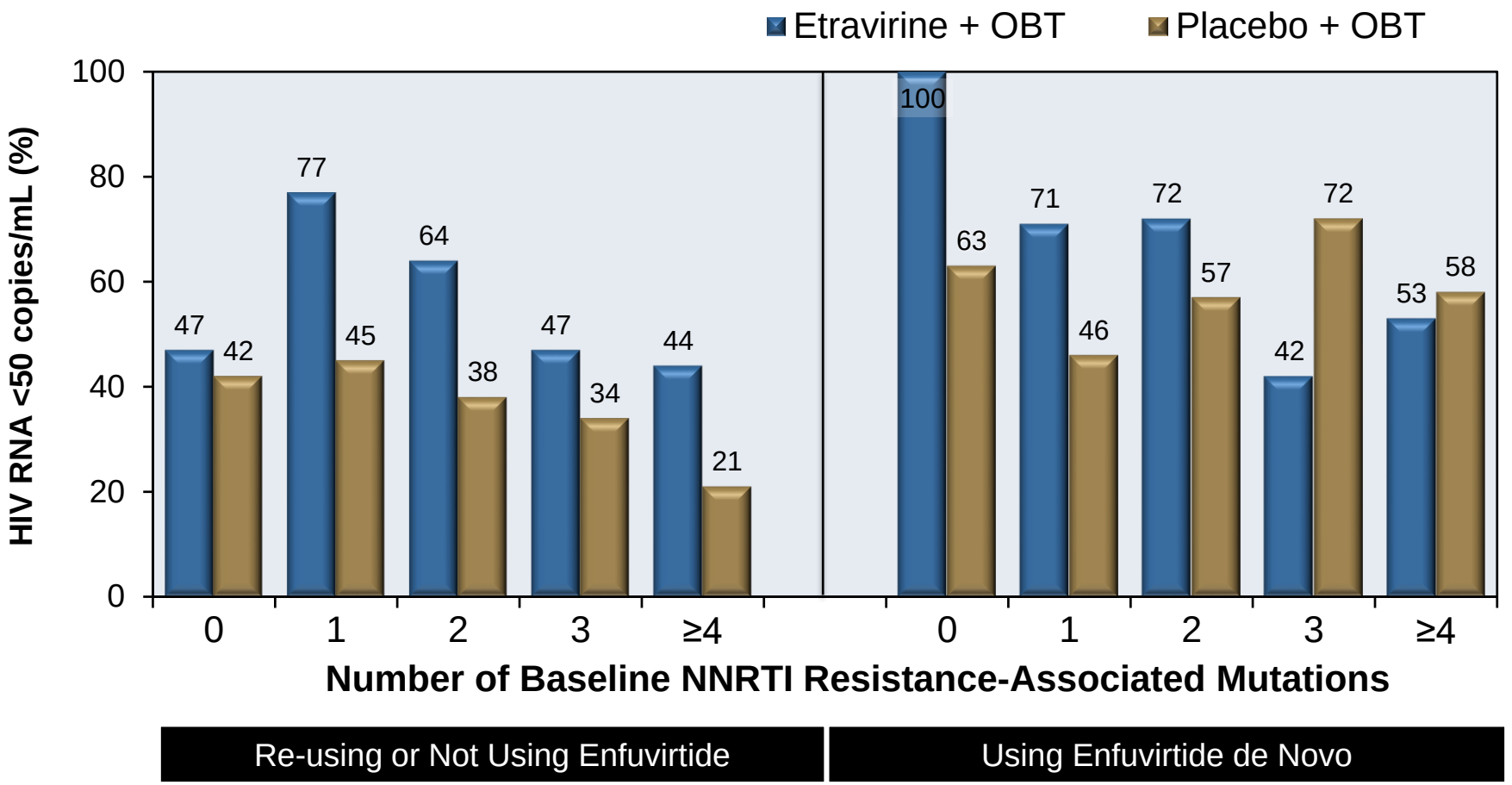


*ITT-TLOVR = Intention to Treat-Time to Loss of Virologic Response.

Source: Madruga JV, et al. Lancet. 2007;370:29-38.

Etravirine in Treatment Experienced
DUET-1: Results

Week 24: Virologic Response (ITT-TLOVR*)



Source: Madruga JV, et al. Lancet. 2007;370:29-38.

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DUET-1: Conclusions

Interpretation: “In treatment-experienced patients with NNRTI resistance, treatment with TMC125 (etravirine) achieved better virological suppression at week 24 than did placebo. The safety and tolerability profile of TMC125 (etravirine) was generally comparable with placebo.”

Source: Madruga JV, et al. Lancet. 2007;370:29-38.

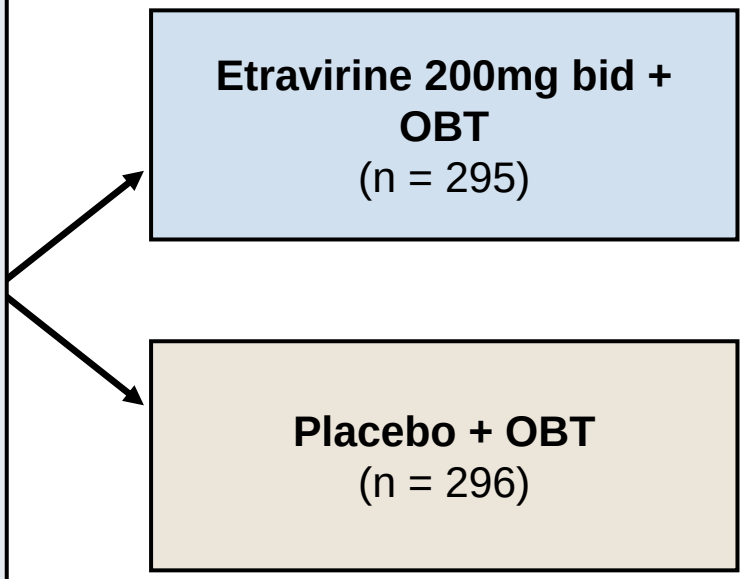
Etravirine in Treatment Experienced

DUET-2 (TMC125-C216)

Etravirine in Treatment Experienced
DUET-2: Study Design

Study Design: DUET-2

- **Background**: Randomized, controlled, double-blind, placebo-controlled phase 3 trial evaluating the long-term efficacy, tolerability, and safety of etravirine in treatment-experienced adults with HIV
- **Inclusion Criteria (n = 591)**
  - Age ≥18 years
  - On stable ARV regimen for ≥8 weeks
  - HIV RNA >5000 copies/mL
  - ≥3 primary PI mutations
  - ≥1 NNRTI resistance-associated mutation
- **Treatment Arms**
  - Etravirine 200 mg BID + OBT*
  - Placebo + OBT*

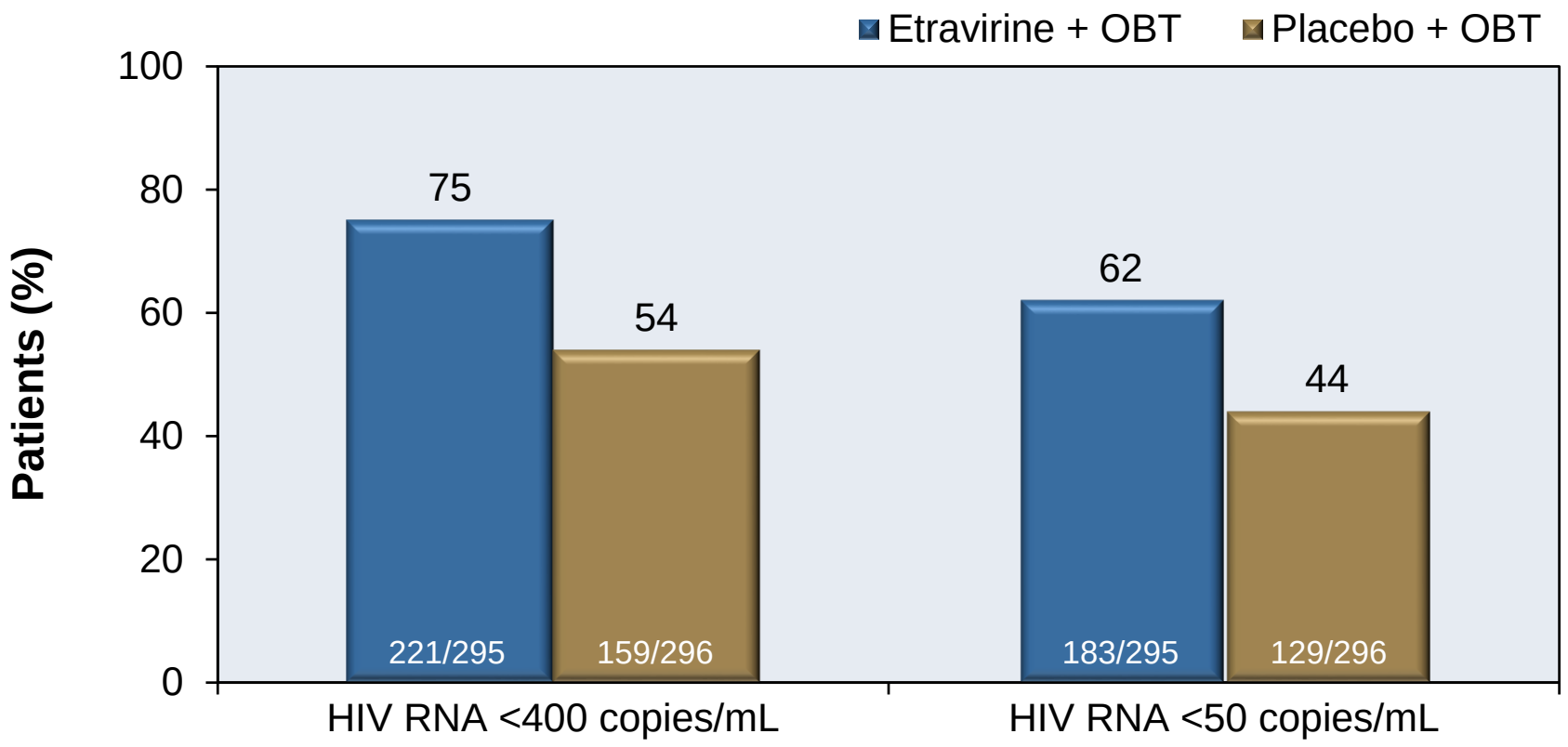


*OBT = NRTIs, Darunavir/r, +/- Enfuvirtide

Source: Lazzarin A, et al. Lancet. 2007;370:39-48.

Etravirine in Treatment Experienced
DUET-2: Results

Week 24: Virologic Response (ITT-TLOVR*)



*ITT-TLOVR = Intention to Treat-Time to Loss of Virologic Response.

Source: Lazzarin A, et al. Lancet. 2007;370:39-48.

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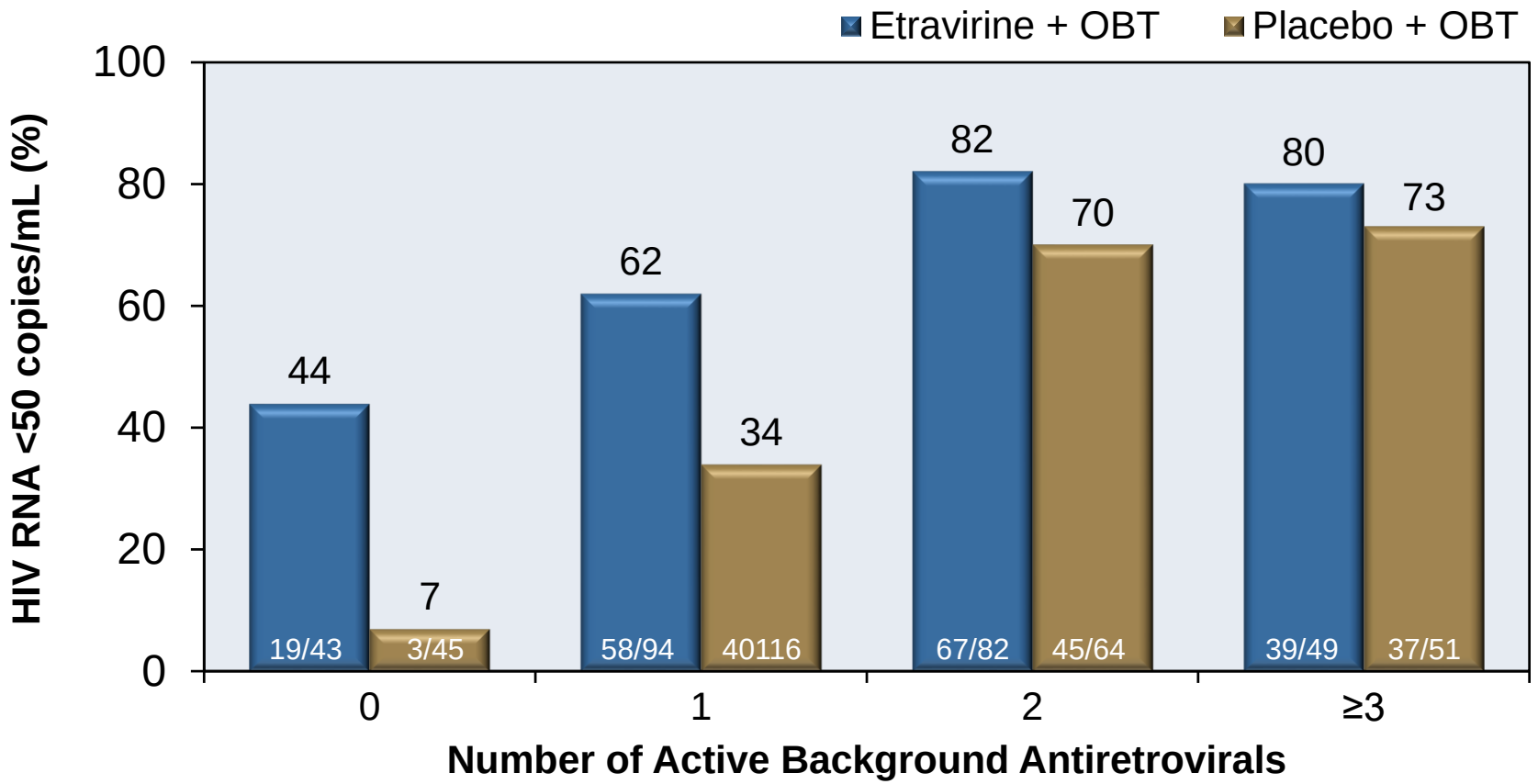
Etravirine in Treatment Experienced
DUET-2: Results

Week 24: Virologic Response (ITT-TLOVR*)



*ITT-TLOVR = Intention to Treat-Time to Loss of Virologic Response.

Source: Lazzarin A, et al. Lancet. 2007;370:39-48.

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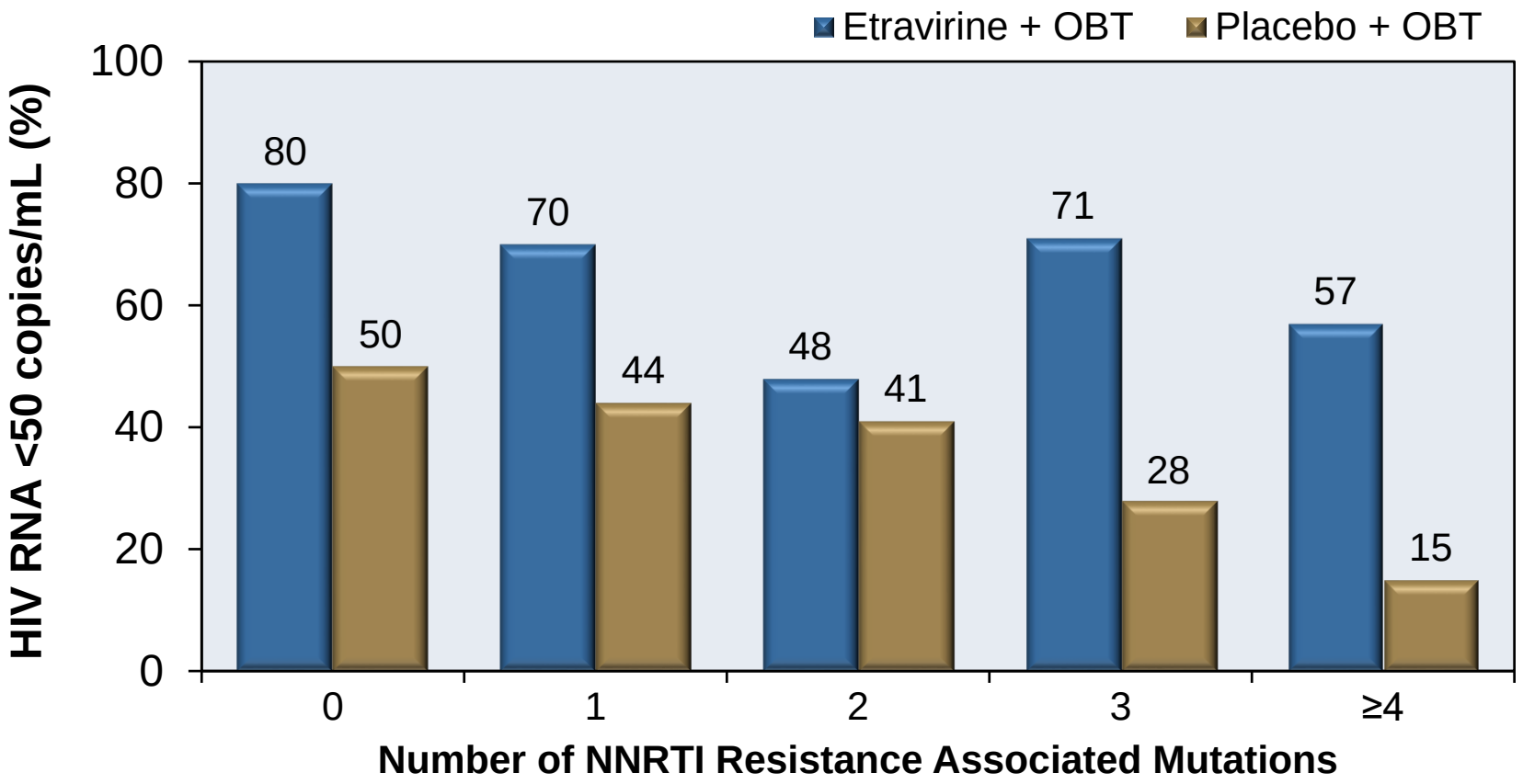
Etravirine in Treatment Experienced
DUET-2: Results

Week 24: Virologic Response (ITT-TLOVR*) in Patients Re-using or Not Using Enfuvirtide



*ITT-TLOVR = Intention to Treat-Time to Loss of Virologic Response.

Source: Lazzarin A, et al. Lancet. 2007;370:39-48.

DUET-2: Conclusions

Interpretation: “In treatment-experienced patients, treatment with TMC125 (etravirine) led to better virological suppression at week 24 than did placebo. The safety and tolerability profile of TMC125 (etravirine) was generally comparable with placebo.”

Source: Lazzarin A, et al. Lancet. 2007;370:39-48.

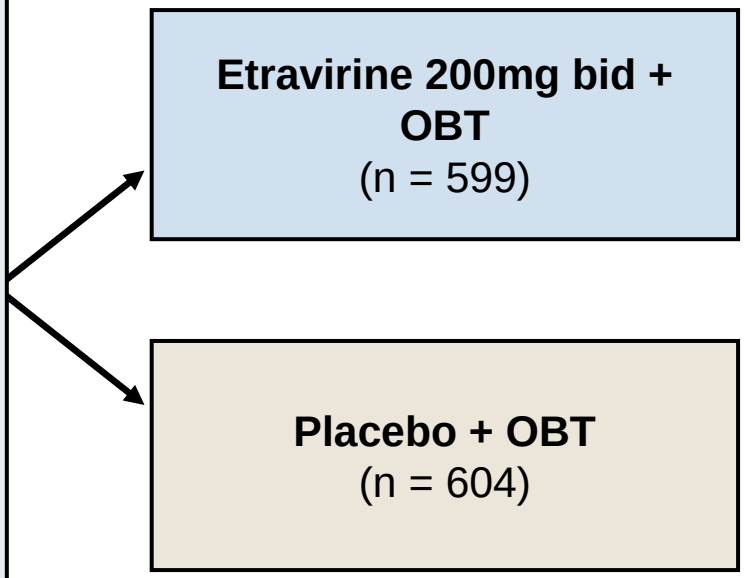
Etravirine in Treatment Experienced

DUET-1 and DUET-2 (Pooled Analysis)

DUET-1 and DUET-2 Pooled Analysis: Study Design

Study Design: DUET-1 and DUET-2

- **Background**: Pooled analysis of 2 randomized, controlled, double-blind, placebo-controlled phase 3 trial evaluating the long-term efficacy, tolerability, and safety of etravirine in treatment-experienced adults with HIV
- **Inclusion Criteria (n = 1203)**
  - Age ≥18 years
  - On stable ARV regimen for ≥8 weeks
  - HIV RNA >5000 copies/mL
  - ≥3 primary PI mutations and ≥1NNRTI resistance-associated mutation
- **Treatment Arms**
  - Etravirine 200 mg BID + OBT*
  - Placebo + OBT*

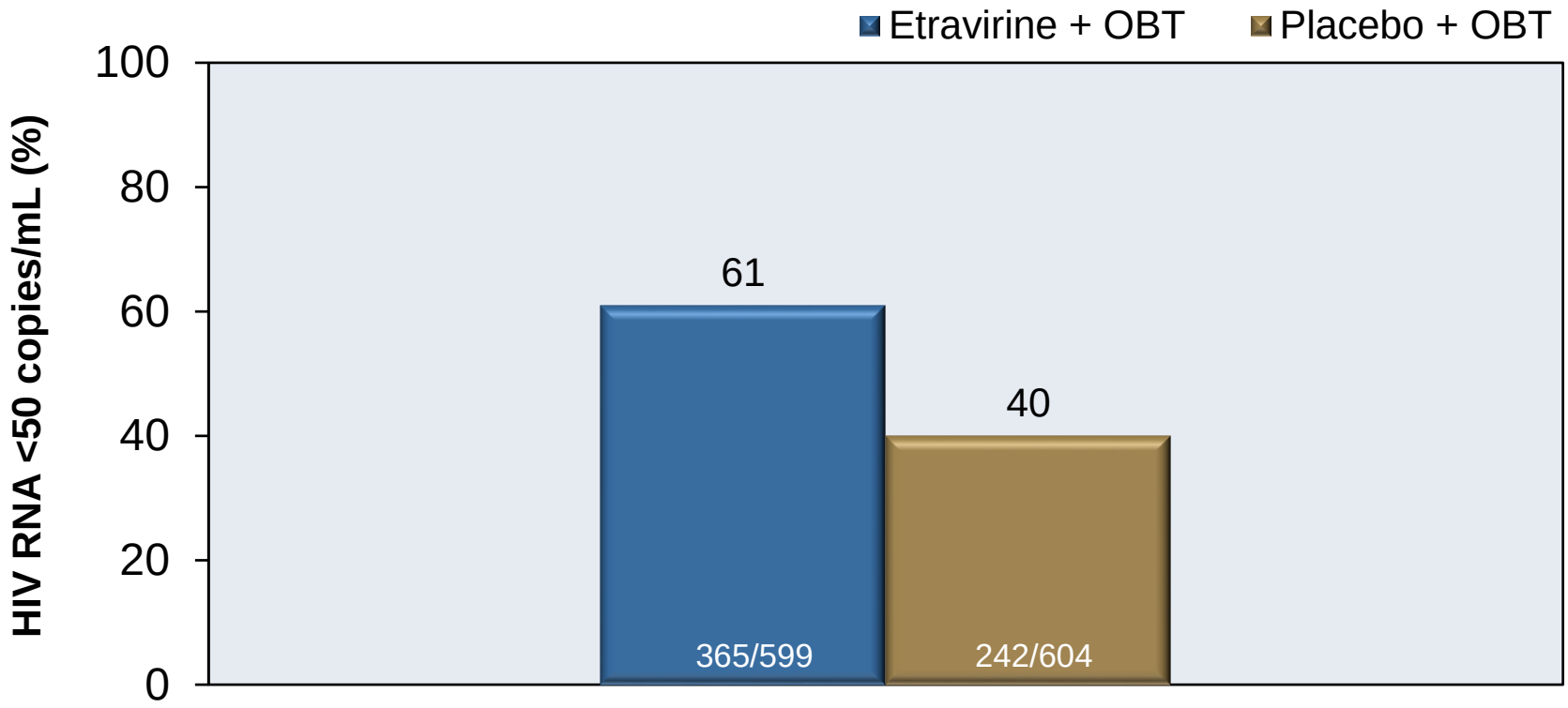


*OBT = NRTIs, Darunavir/r, +/- Enfuvirtide

Source: Lazzarin A, et al. Lancet. 2007;370:39-48.

Etravirine in Treatment Experienced
DUET-1 and DUET-2 Pooled Analysis: Results

Week 48: Virologic Response (ITT-TLOVR*)

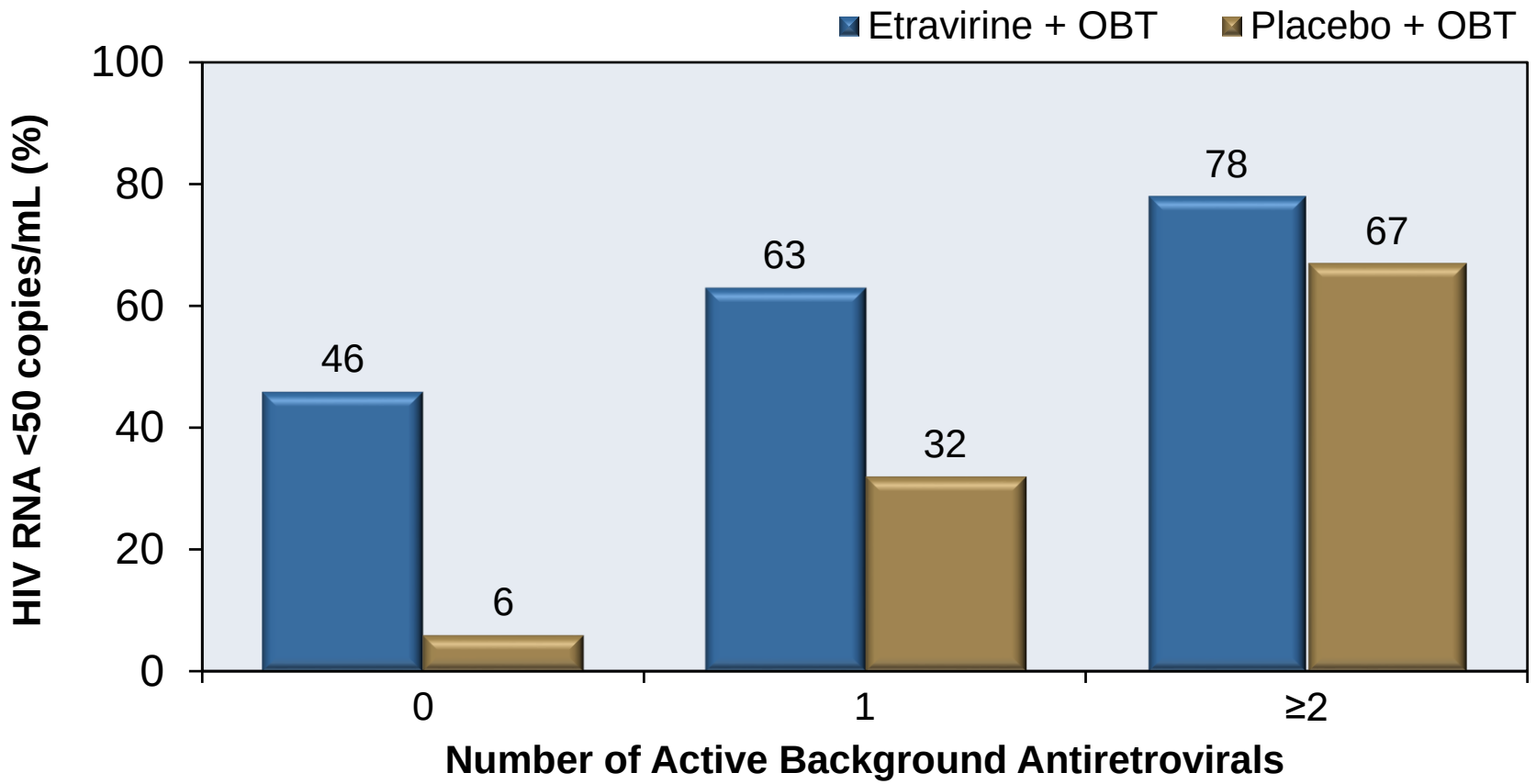


*ITT-TLOVR = Intention to Treat-Time to Loss of Virologic Response.

Source: Katlama C, et al. AIDS. 2009;23:2289-300.

Etravirine in Treatment Experienced
DUET-1 and DUET-2 Pooled Analysis: Results

Week 48: Virologic Response (ITT-TLOVR*), by Number of Active ARVs

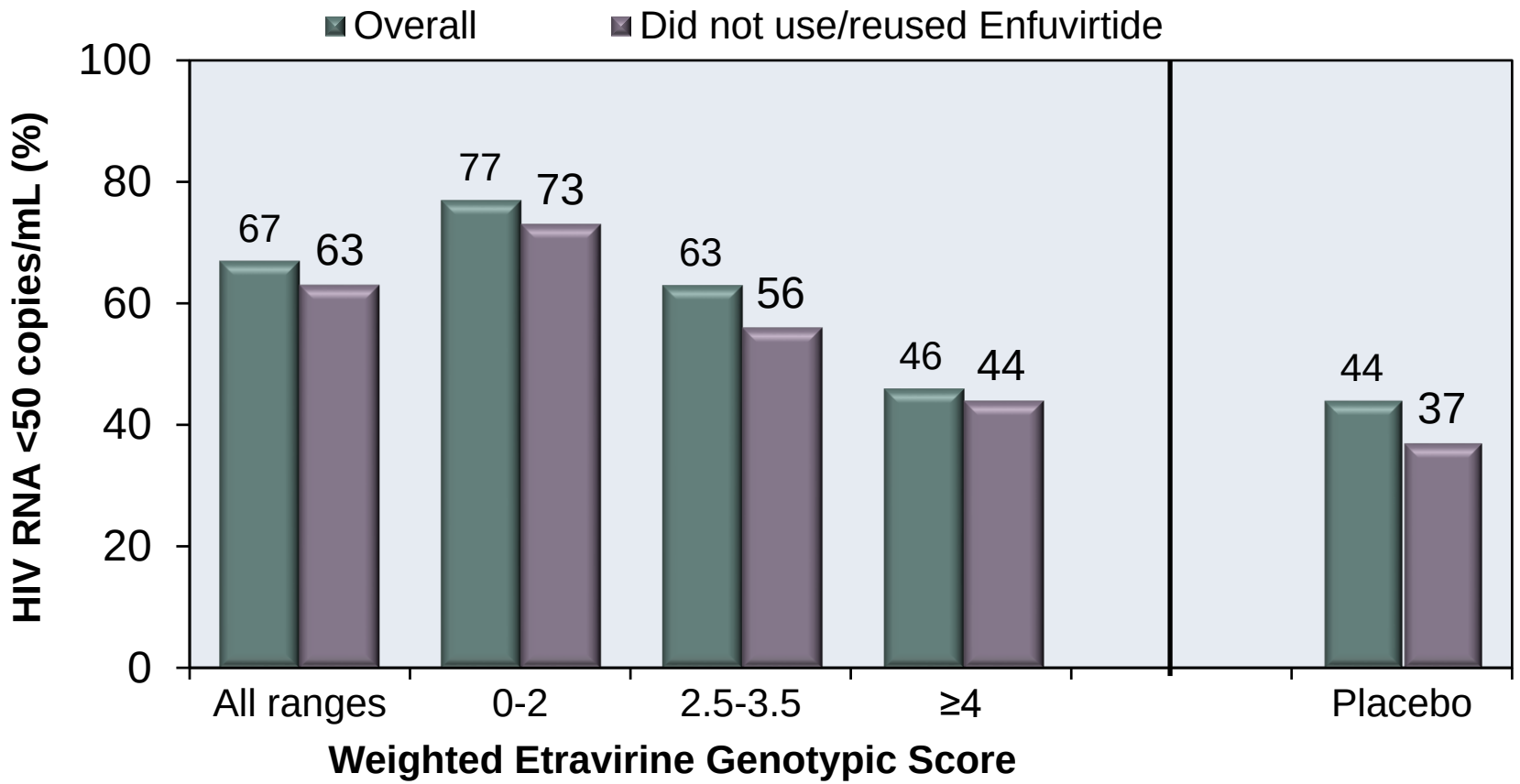


*ITT-TLOVR = Intention to Treat-Time to Loss of Virologic Response.

Source: Katlama C, et al. AIDS. 2009;23:2289-300.

Etravirine in Treatment Experienced
DUET-1 and DUET-2: Pooled Analysis

Week 48: Virologic Response in Etravirine Group, by Weighted Genotypic Score



Source: Katlama C, et al. AIDS. 2009;23:2289-300.

Etravirine in Treatment Experienced
DUET-1 and DUET-2 Pooled Analysis: Conclusions

Conclusion: “At 48 weeks, treatment-experienced patients receiving etravirine plus background regimen had statistically superior and durable virologic responses (viral load less than 50 copies/ml) than those receiving placebo plus background regimen, with comparable tolerability and no new safety signals reported since week 24.”

Source: Katlama C, et al. AIDS. 2009;23:2289-300.

ETV+ DRV/r + RAL in Treatment-Experienced Patients

TRIO Trial

Etravirine + Darunavir/r + Raltegravir
TRIO: Study Design

Study Design: TRIO

- **Background**: Phase 2, non-comparative trial assessing safety and efficacy of an antiretroviral regimen containing etravirine, darunavir boosted with ritonavir, and raltegravir in adults with HIV and multidrug-resistant virus
- **Inclusion Criteria (n = 103)**
  - Age ≥18 years
  - On stable ARV regimen for ≥8 weeks
  - HIV RNA >1000 copies/ml
  - Mutations allowed: ≥3 PI, ≥3 NRTI, ≤ 3NNRTI
  - Naïve to etravirine, darunavir, and raltegravir
- **Treatment Arms**
  - Etravirine 200 mg bid + Darunavir 600 mg BID + Ritonavir 100mg bid + Raltegravir 400 mg bid + optimized background regimen (OBR)

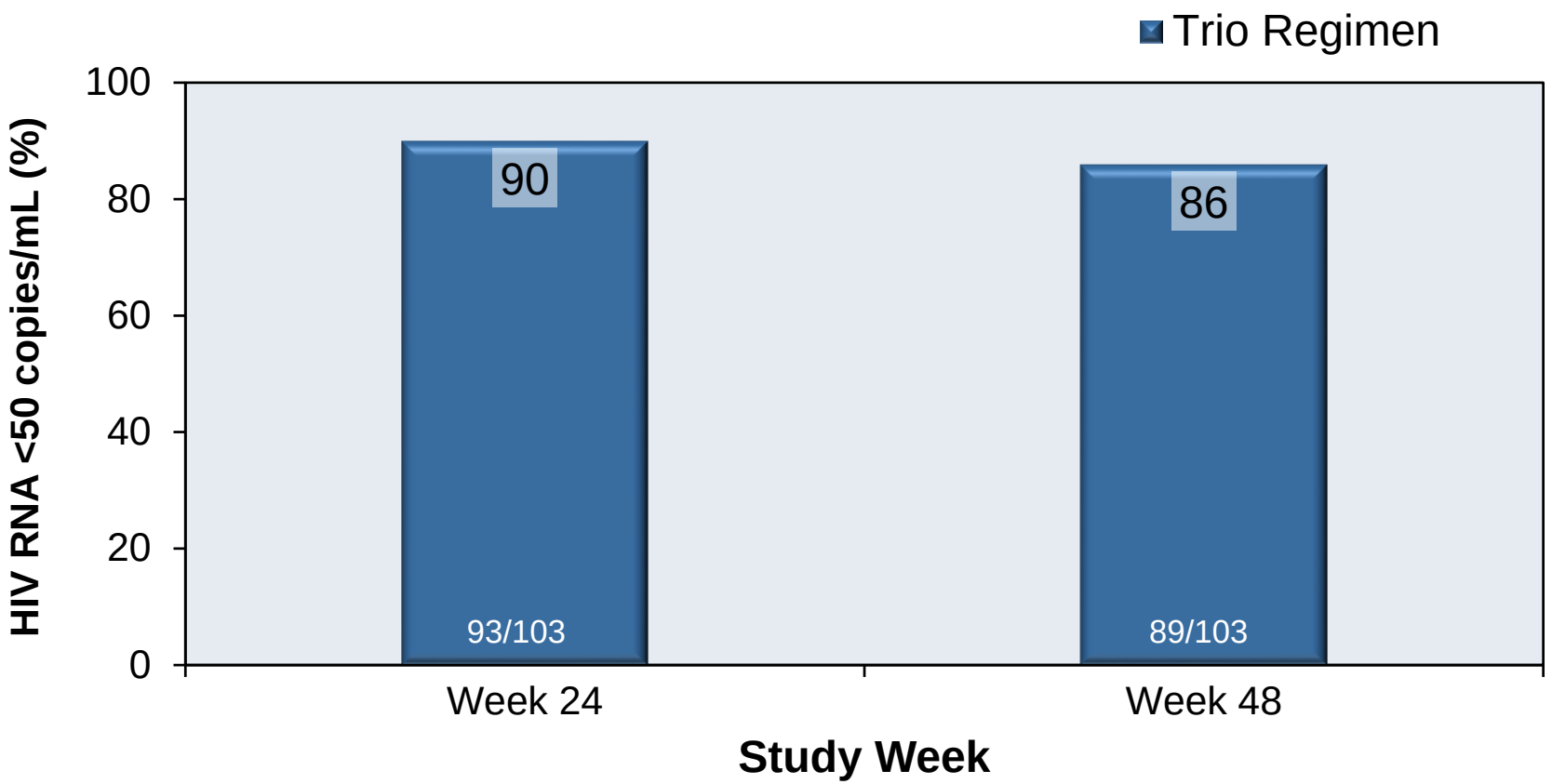
Trio Regimen
Etravirine +
Darunavir + Ritonavir +
Raltegravir
+ OBT
(n = 103)

*OBT = NRTIs +/- Enfuvirtide

Source: Yazdanpanah Y, et al. Clin Infect Dis. 2009;49:1441-9.

Etravirine + Darunavir/r + Raltegravir
TRIO: Result

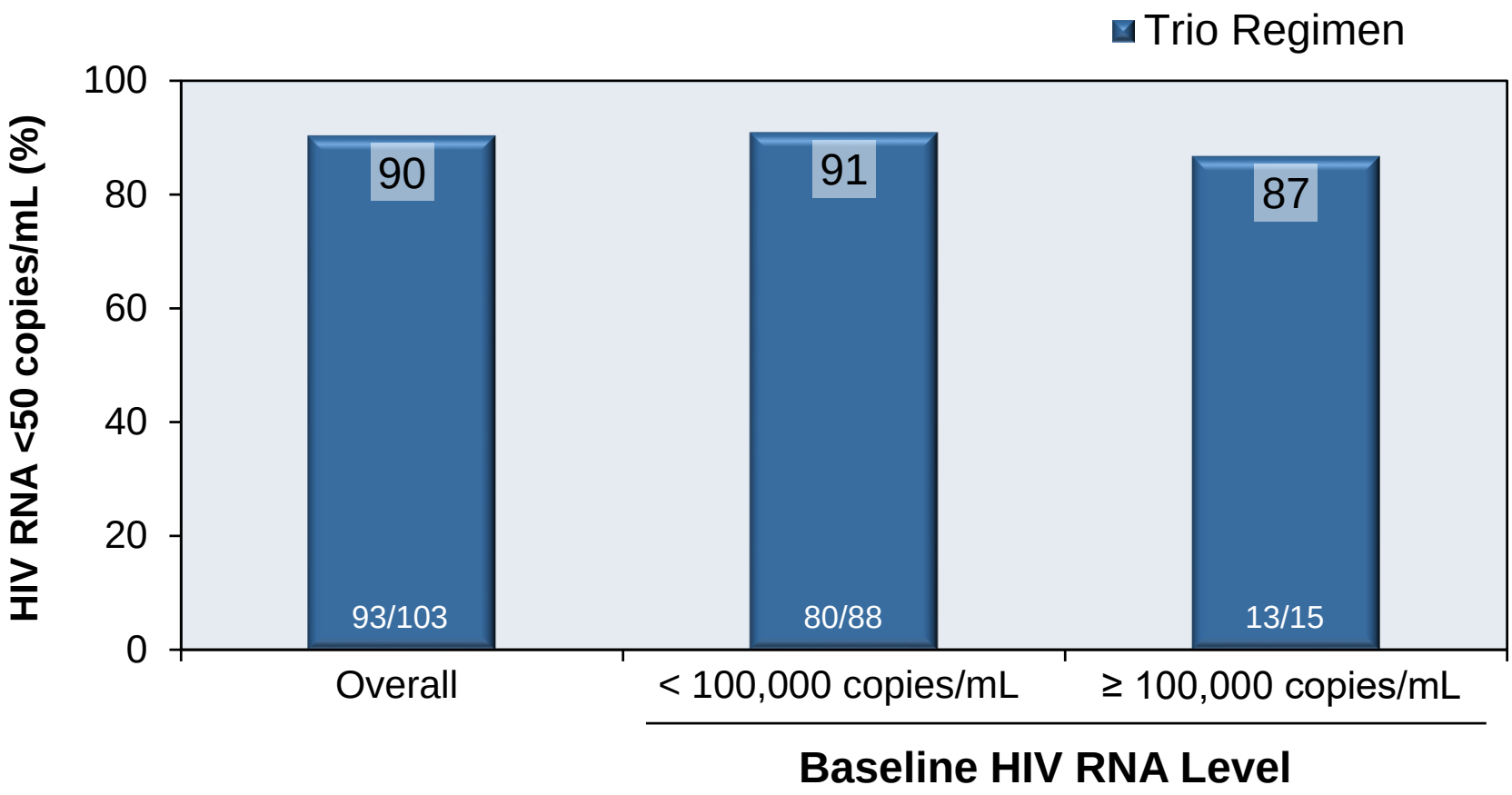
Week 24 and 48: Virologic Response (Intention-to-treat Analysis)



Source: Yazdanpanah Y, et al. Clin Infect Dis. 2009;49:1441-9.

Etravirine + Darunavir/r + Raltegravir
TRIO: Result

Week 24: Virologic Response (ITT Analysis), by Baseline HIV RNA



Source: Yazdanpanah Y, et al. Clin Infect Dis. 2009;49:1441-9.

Etravirine + Darunavir/r + Raltegravir

TRIO: Conclusions

Conclusion: “In patients infected with multidrug-resistant virus who have few remaining treatment options, the combination of raltegravir, etravirine, and darunavir/ritonavir is well tolerated and is associated with a rate of virologic suppression similar to that expected in treatment-naive patients.”

Source: Yazdanpanah Y, et al. Clin Infect Dis. 2009;49:1441-9.

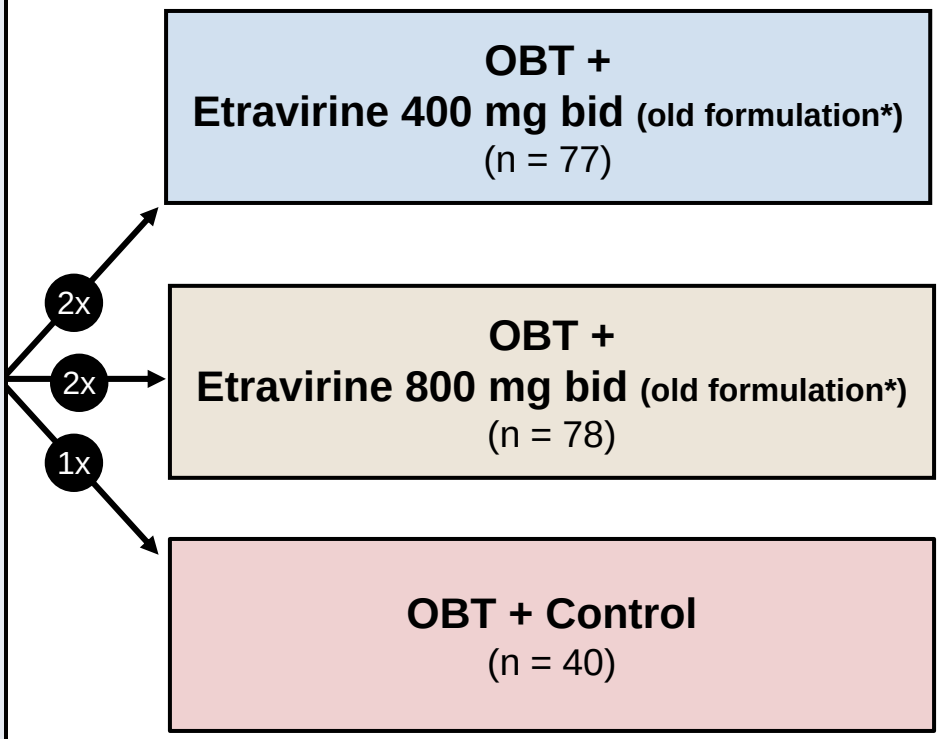
Etravirine in Treatment-Experienced Patients

Study TMC125-C223

Etravirine (formerly TMC125) in Patients with Highly Resistant HIV
Study TMC125-C223: Study Design

Study Design: TMC125-C223

- **Background**: Randomized, controlled, partially-blind, phase 2b trial evaluating the safety and efficacy of phase 2b formulation of etravirine combined with optimized background therapy (OBT) compared with a standard-of-care regimen
- **Inclusion Criteria (n = 199)**
  - Adults with HIV
  - HIV RNA >1,000 copies/mL
  - ≥3 NNRTI resistance mutations
- **Treatment Arms**
  - OBT + *Etravirine 400 mg bid
  - OBT + *Etravirine 800 mg bid
  - OBT + *Control (included at least 3 ARVs: NRTIs, PIs, and/or Enfuvirtide)

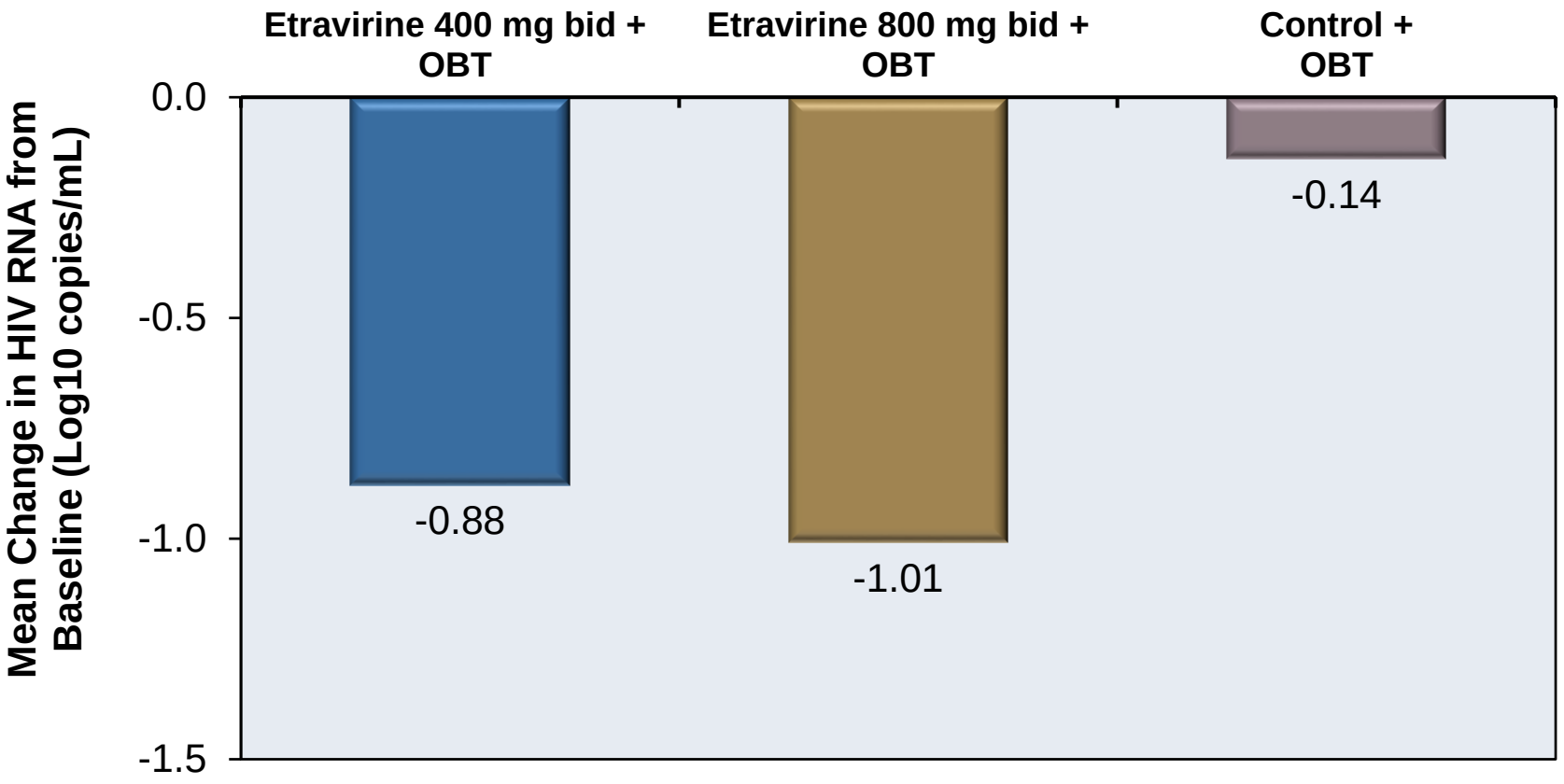


*Old formulation of etravirine 800 mg equivalent to 200 mg of FDA-approved formulation of etravirine

Source: Cohen CJ, et al. AIDS. 2009;23:423-6.

Etravirine (formerly TMC125) in Patients with Highly Resistant HIV
Study TMC125-C223: Results

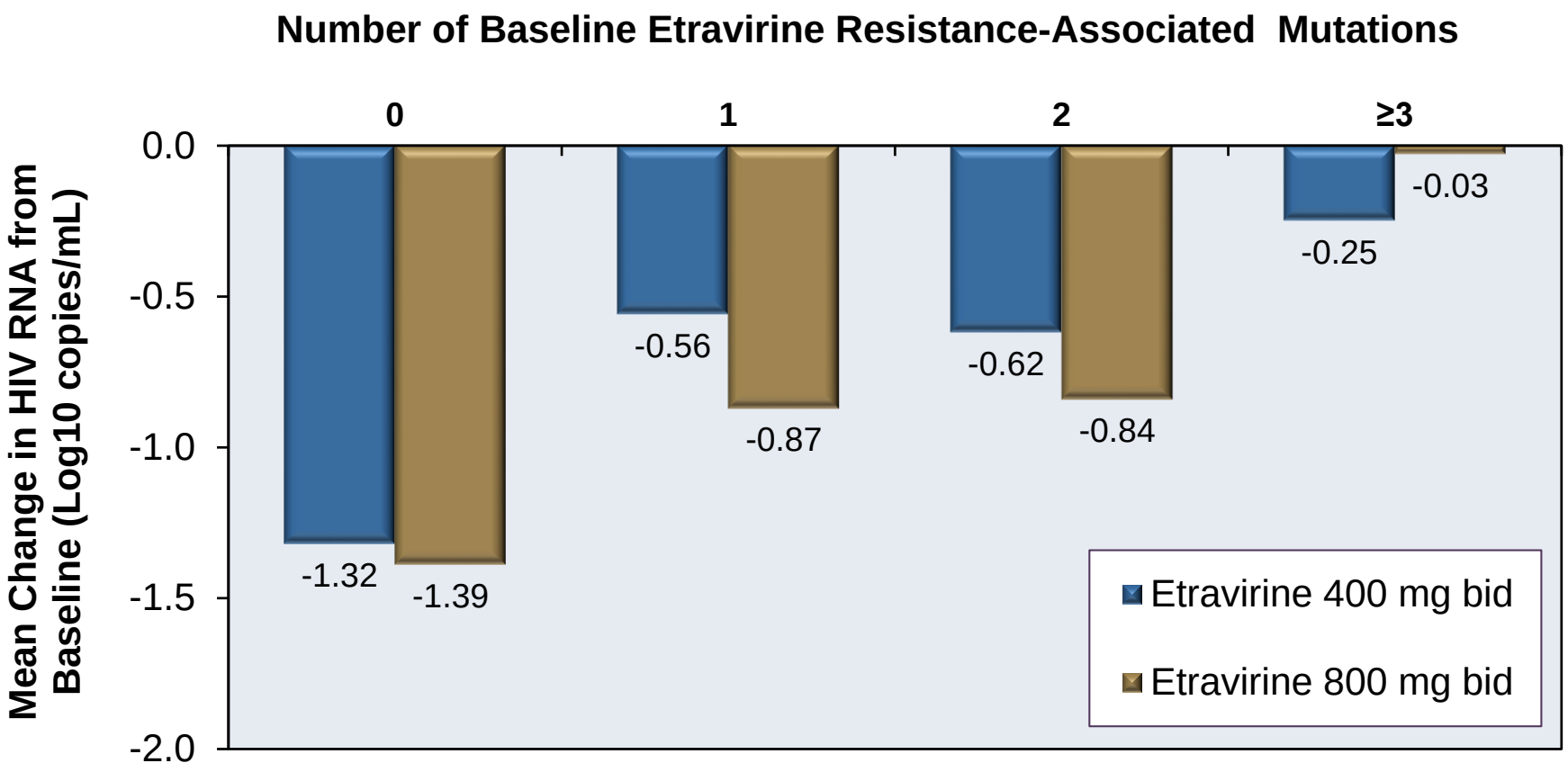
Week 48: Change in HIV RNA Level



Source: Cohen CJ, et al. AIDS. 2009;23:423-6.

Etravirine (formerly TMC125) in Patients with Highly Resistant HIV
Study TMC125-C223: Results

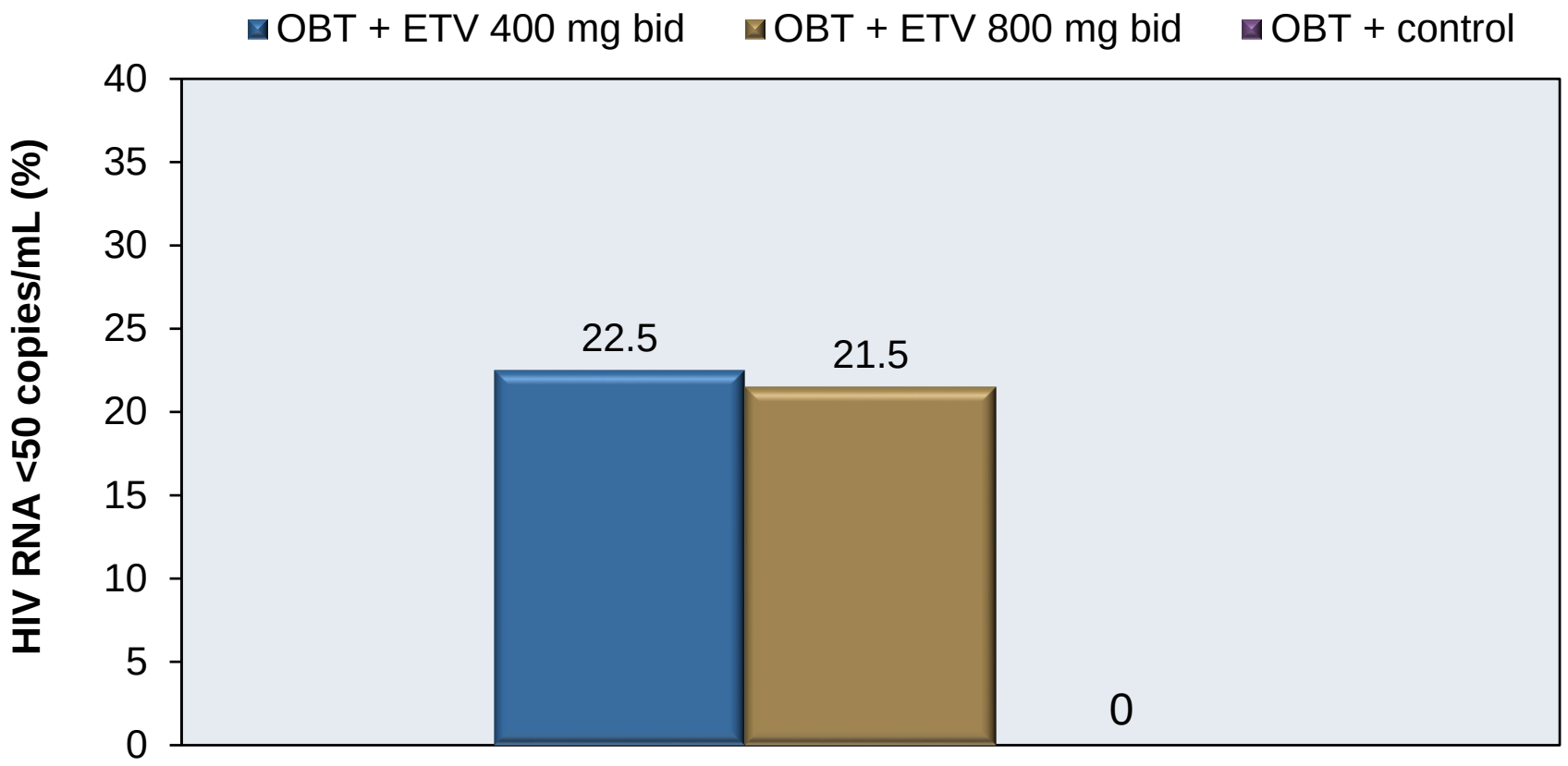
Week 48: Change in HIV RNA, by Baseline Etravirine Mutations



Source: Cohen CJ, et al. AIDS. 2009;23:423-6.

Etravirine (formerly TMC125) in Patients with Highly Resistant HIV
Study TMC125-C223: Results

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



Source: Cohen CJ, et al. AIDS. 2009;23:423-6.

Etravirine (formerly TMC125) in Patients with Highly Resistant HIV
Study TMC125-C223: Week 24 Conclusions

Conclusion: “Etravirine demonstrated higher efficacy than control, irrespective of the number of detectable nonnucleoside reverse transcriptase inhibitor resistance-associated mutations.”

Source: Cohen CJ, et al. AIDS. 2009;23:423-6.

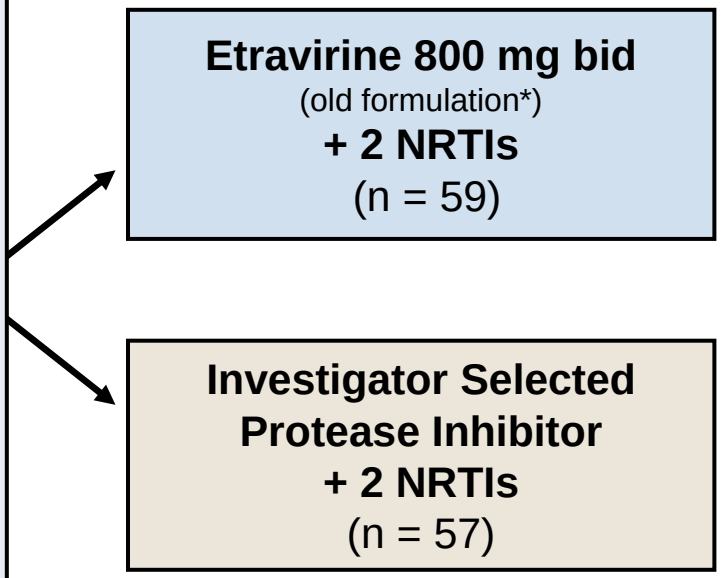
Etravirine versus Protease Inhibitor in ARV-Experienced

TMC 125-C227

Etravirine *versus* Protease Inhibitor in ARV-Experienced TMC125-C227: Study Design

Study Design: TMC125-C227

- **Background**: Randomized, controlled, open-label phase 2 trial evaluating the safety and efficacy of etravirine (formerly TMC125) in PI-naïve patients with NNRTI resistance
- **Inclusion Criteria (n = 116)**
  - Age >18 years
  - HIV RNA >1,000 copies/mL
  - Documented genotypic NNRTI resistance
  - PI naïve
- **Treatment Arms**
  - Etravirine 800 mg bid + 2NRTIs
  - Investigator-selected PI + 2NRTIs

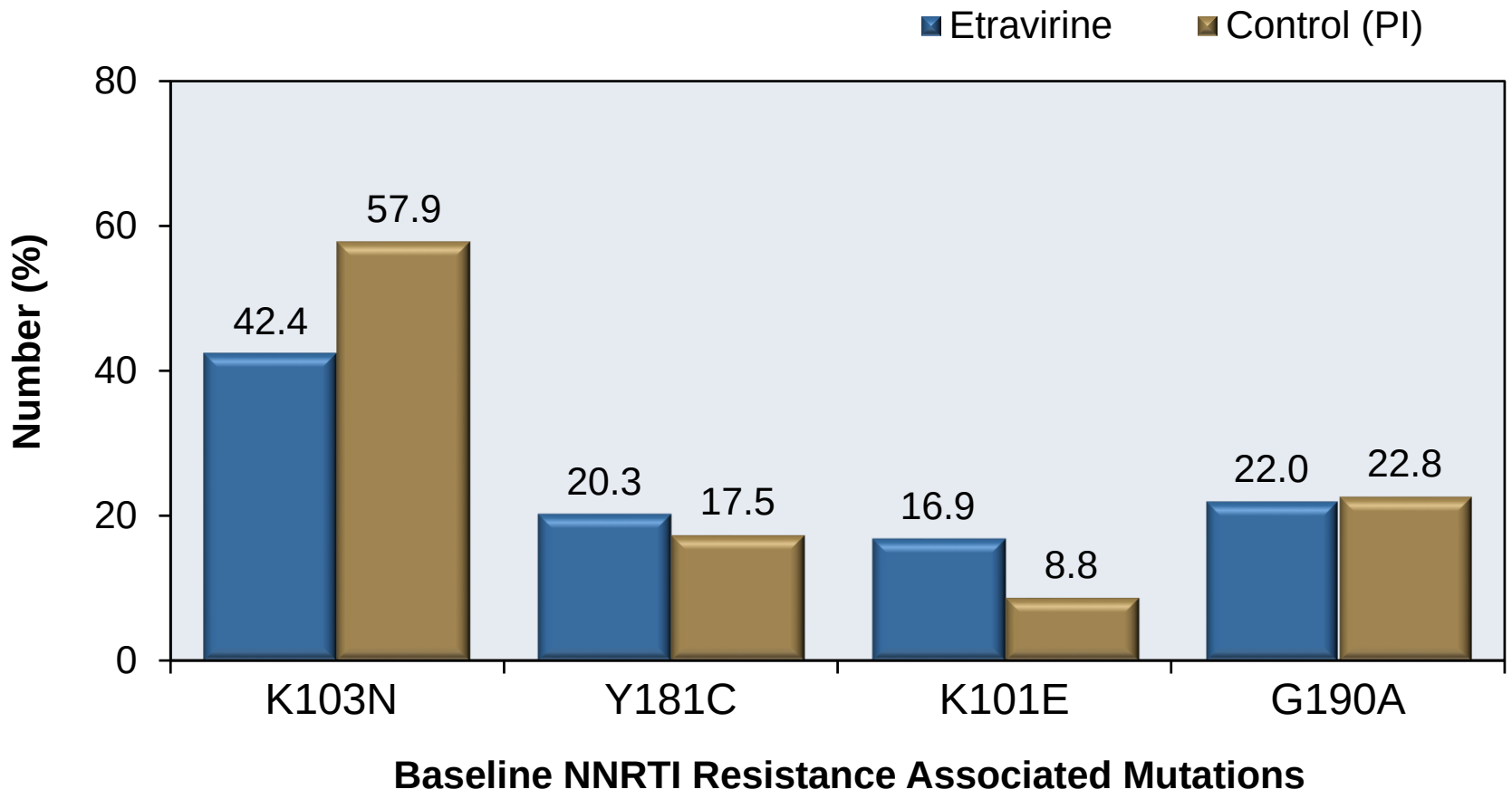


*Note: Old formulation of 800 mg bid equivalent to FDA-approved etravirine dose of 200 mg bid. Initial study planned for 48 weeks, but enrollment stopped prematurely and etravirine treatment discontinued after median 14.3 weeks due to suboptimal virologic response.

Source: Ruxrungtham K, et al. HIV Med. 2008;9:883-96.

Etravirine *versus* Protease Inhibitor in ARV-Experienced TMC125-C227: Study Design

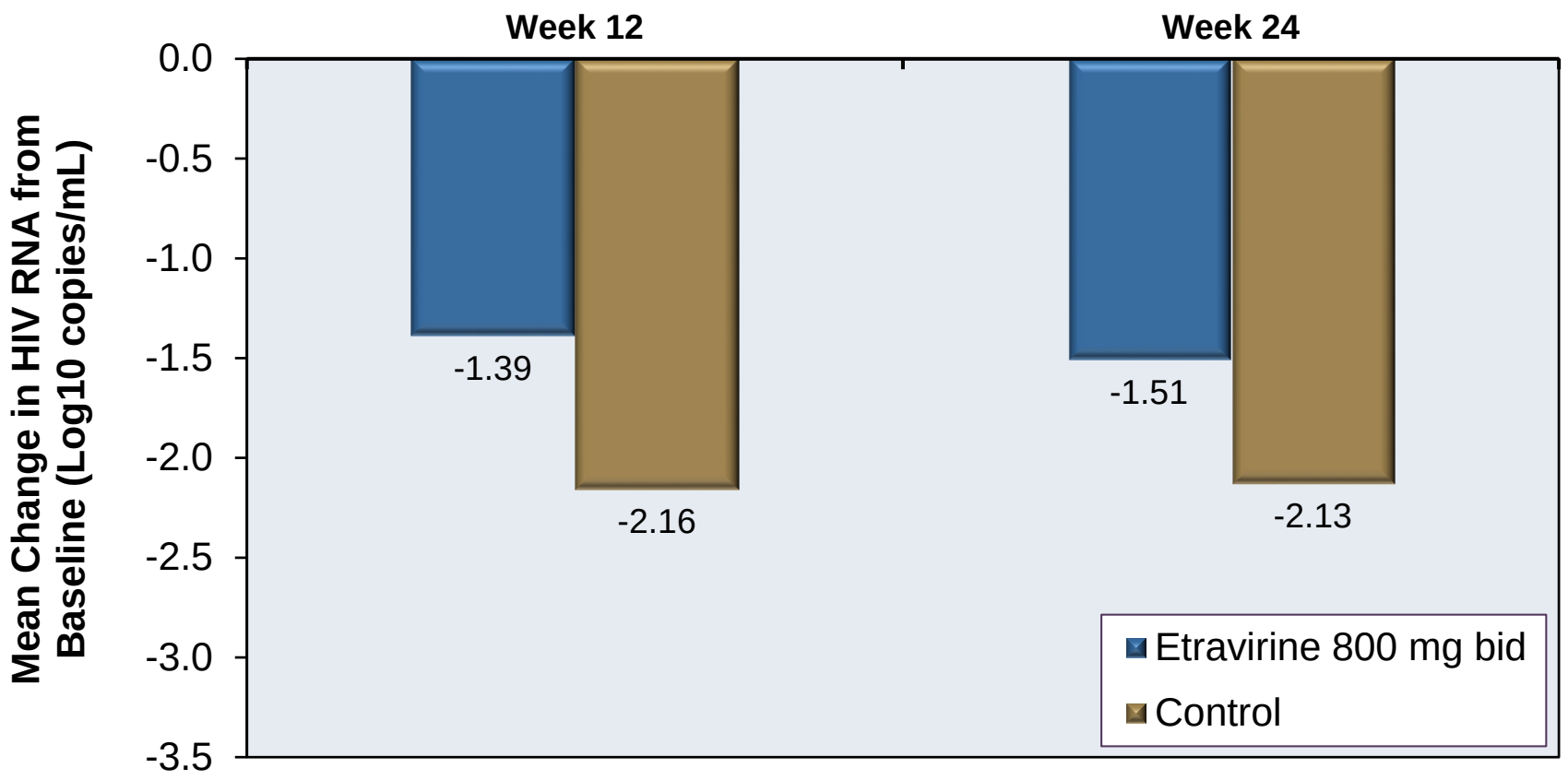
Prevalence of Baseline NNRTI Resistance Mutations



Source: Ruxrungtham K, et al. HIV Med. 2008;9:883-96.

Etravirine in Patients with Highly Resistant HIV
TMC125-C223: Results

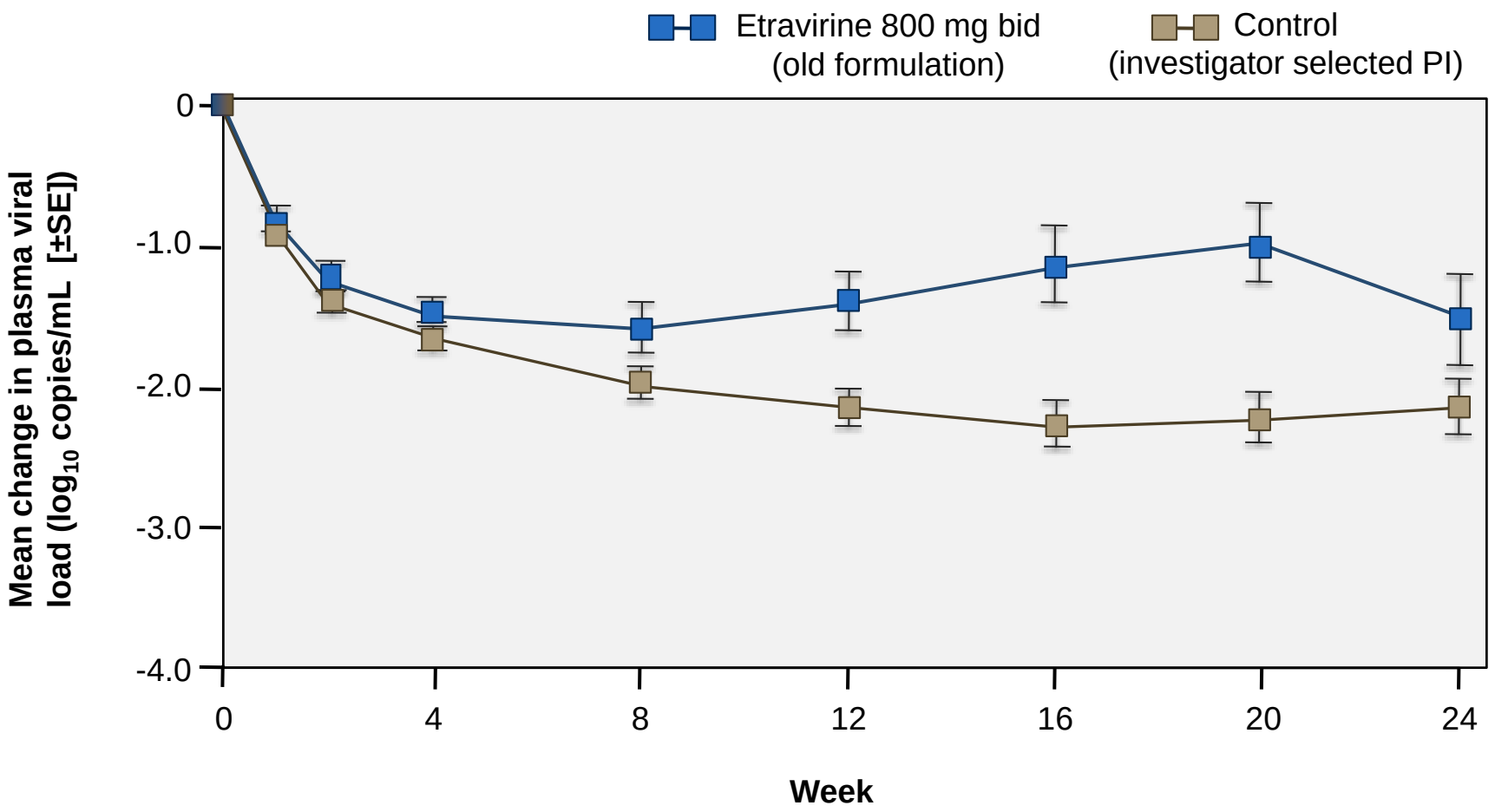
Weeks 12 and 24: Change in HIV RNA



Source: Ruxrungtham K, et al. HIV Med. 2008;9:883-96.

Etravirine *versus* Protease Inhibitor in ARV-Experienced TMC125-C227: Results

Week 24: Mean Change of HIV RNA From Baseline (observed data)



Source: Ruxrungtham K, et al. HIV Med. 2008;9:883-96.

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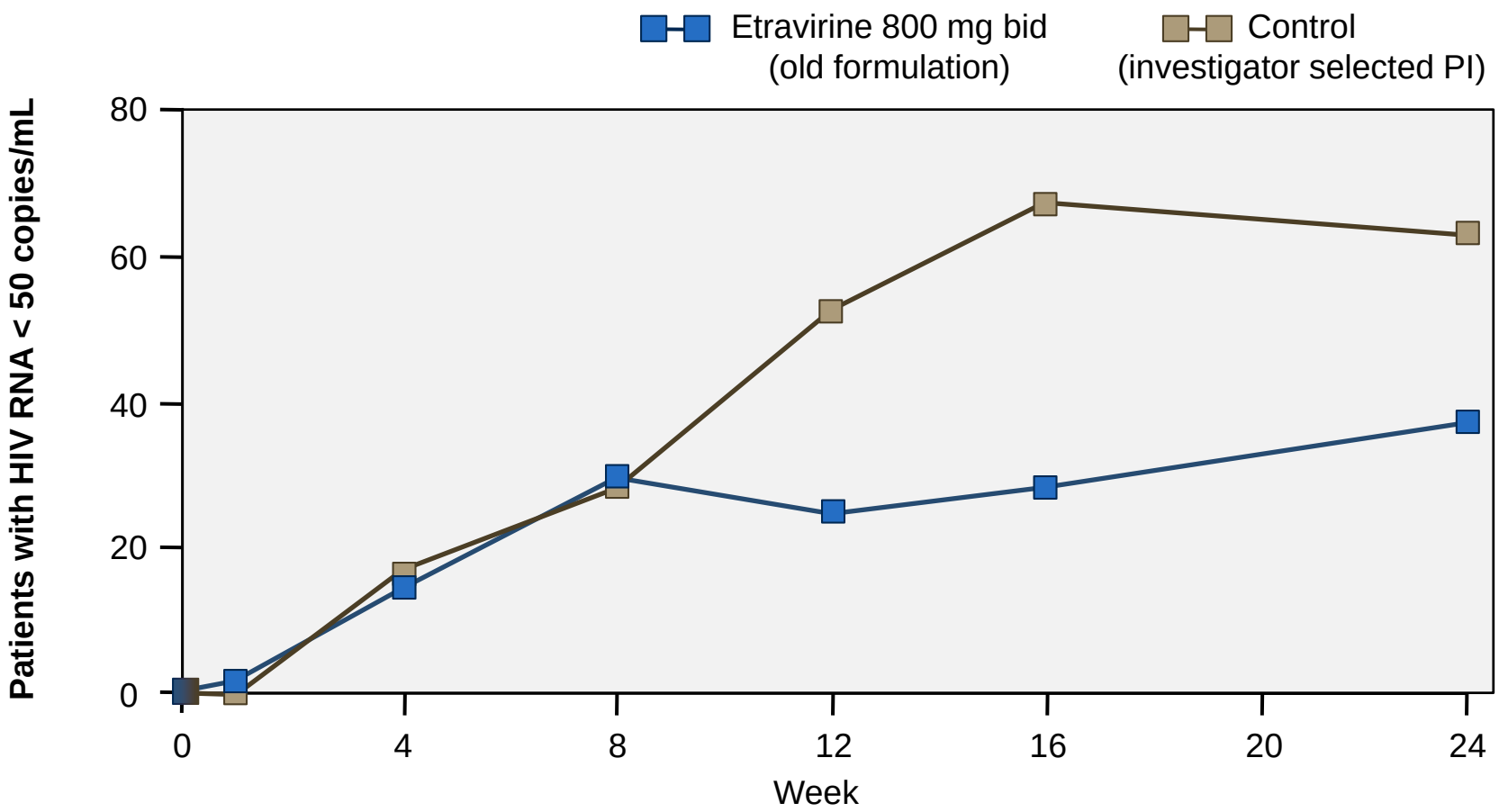
Etravirine *versus* Protease Inhibitor in ARV-Experienced TMC125-C227: Results

Week 24: Proportion of Patients with HIV RNA Less than 50 copies/mL



Source: Ruxrungtham K, et al. HIV Med. 2008;9:883-96.

Etravirine *versus* Protease Inhibitor in ARV-Experienced TMC125-C227: Conclusions

Conclusions: “In a PI-naive population, with baseline NRTI and NNRTI resistance and NRTI recycling, TMC125 (etravirine) was not as effective as first use of a PI. Therefore the use of TMC125 (etravirine) plus NRTIs alone may not be optimal in PI naive patients with first-line virological failure on an NNRTI-based regimen. Baseline two-class resistance, rather than pharmacokinetics or other factors, was the most likely reason for suboptimal responses.”

Source: Ruxrungtham K, et al. HIV Med. 2008;9:883-96.

Etravirine in Treatment-Experienced Children and Adolescents

PIANO Trial

Etravirine in Treatment-Experienced Children & Adolescents
PIANO: Study Design

Study Design: PIANO

- **Background**: Phase 2, single-arm trial assessing safety and efficacy of etravirine in treatment-experienced, HIV-infected patients
- **Inclusion Criteria (n = 101)**
  - Children ≥6 and <12 years
  - Adolescents ≥12 and <18 years old
  - Treatment-experienced
  - No resistance to etravirine
- **Treatment Arms**
  - Etravirine 5.2 mg/kg bid + Investigator-selected optimized background regimen (OBR)

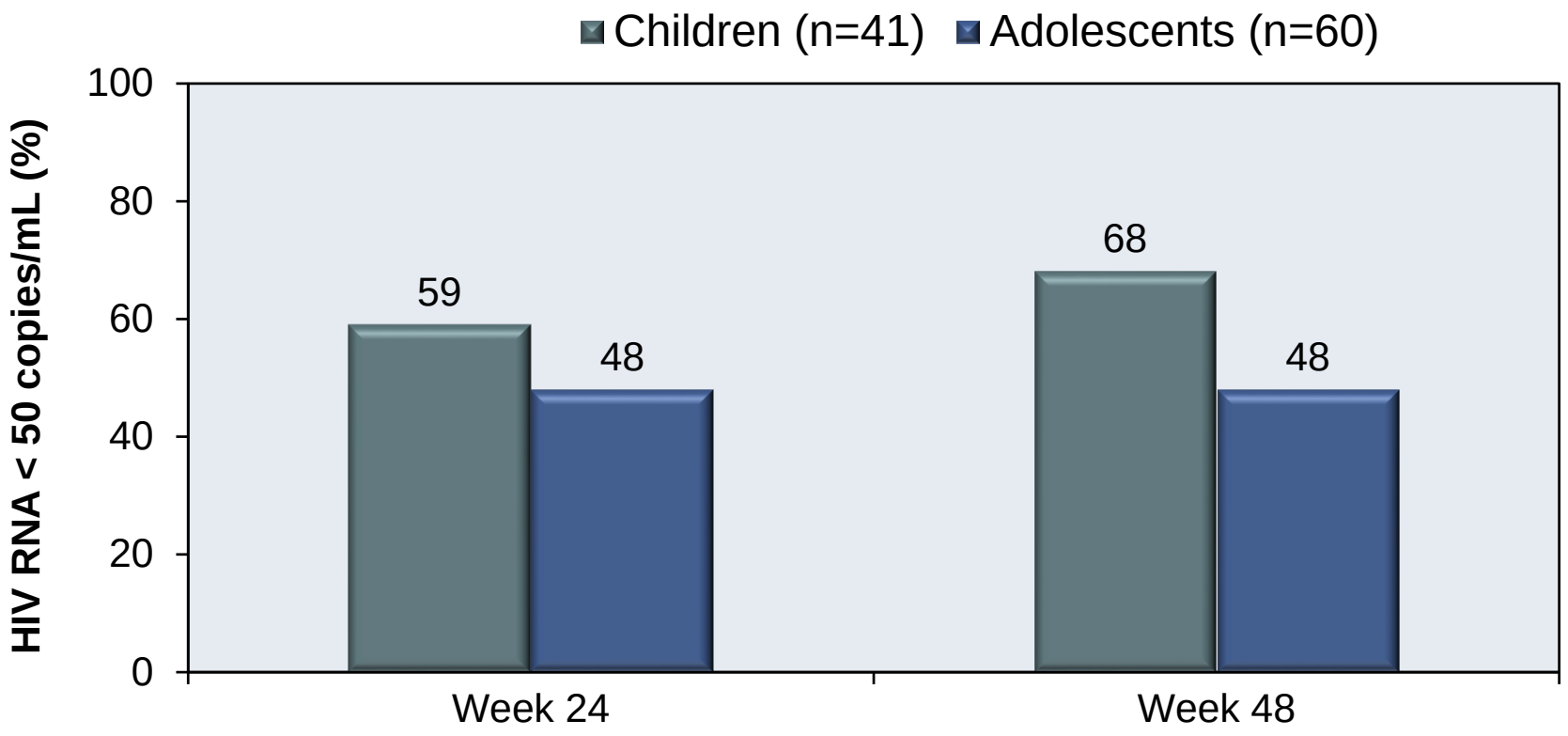
→ **Etravirine 5.2 mg/kg bid + OBR** (n = 101)

*OBT = ≥ 2 active ARVs, including a ritonavir-boosted PI and NRTIs +/- Enfuvirtide +/- Raltegravir

Source: Tudor-Williams G, et al. HIV Med. 2014;15:513-24.

Etravirine in Treatment-Experienced Children & Adolescents
PIANO: Result

Week 24 and 48: Virologic Response (ITT Analysis, N=F)*



*ITT: Intent-to-Treat, N=F: Noncompleter=Failure

Source: Tudor-Williams G, et al. HIV Med. 2014;15:513-24.

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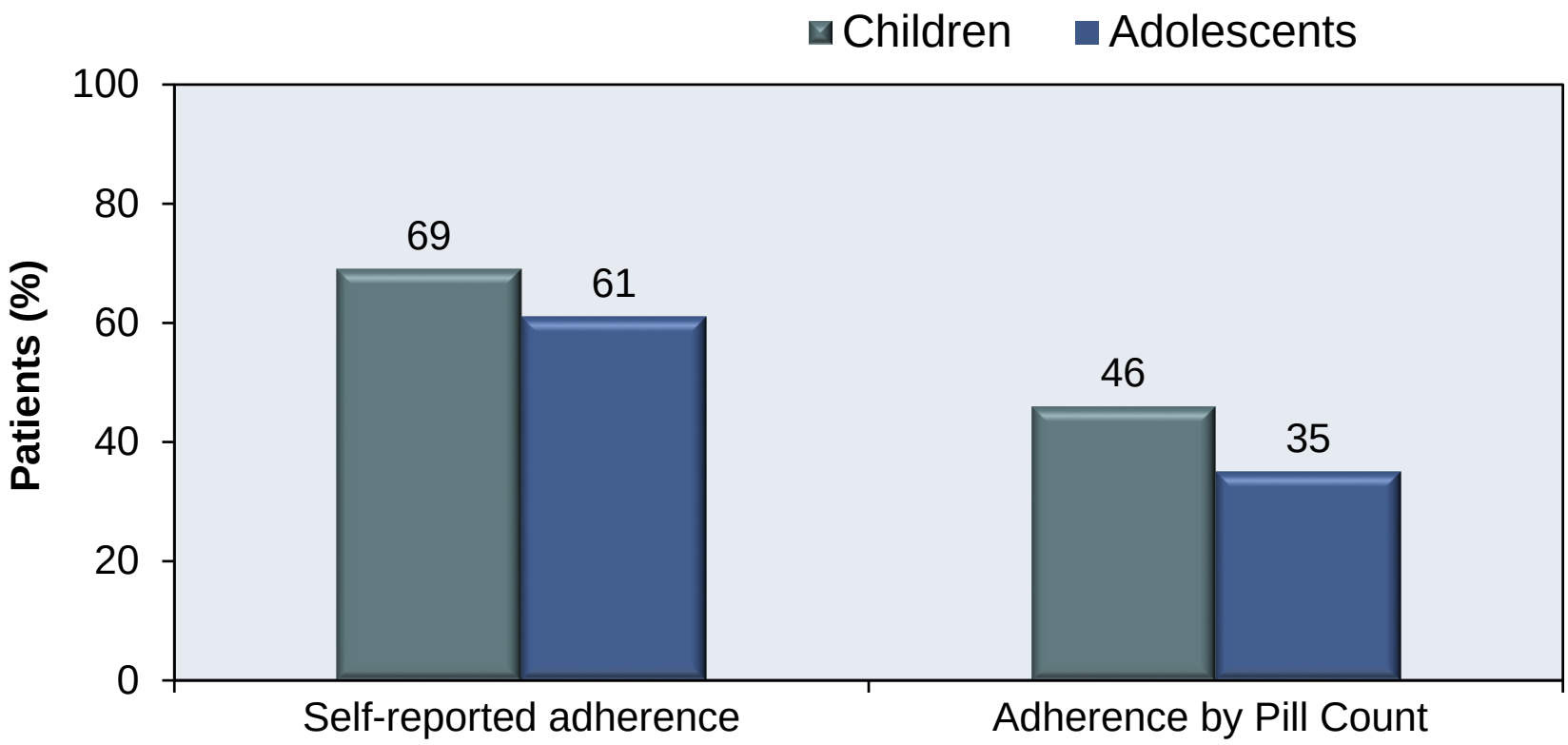
Etravirine in Treatment-Experienced Children & Adolescents

PIANO: Result

Week 48: Measures of Adherence

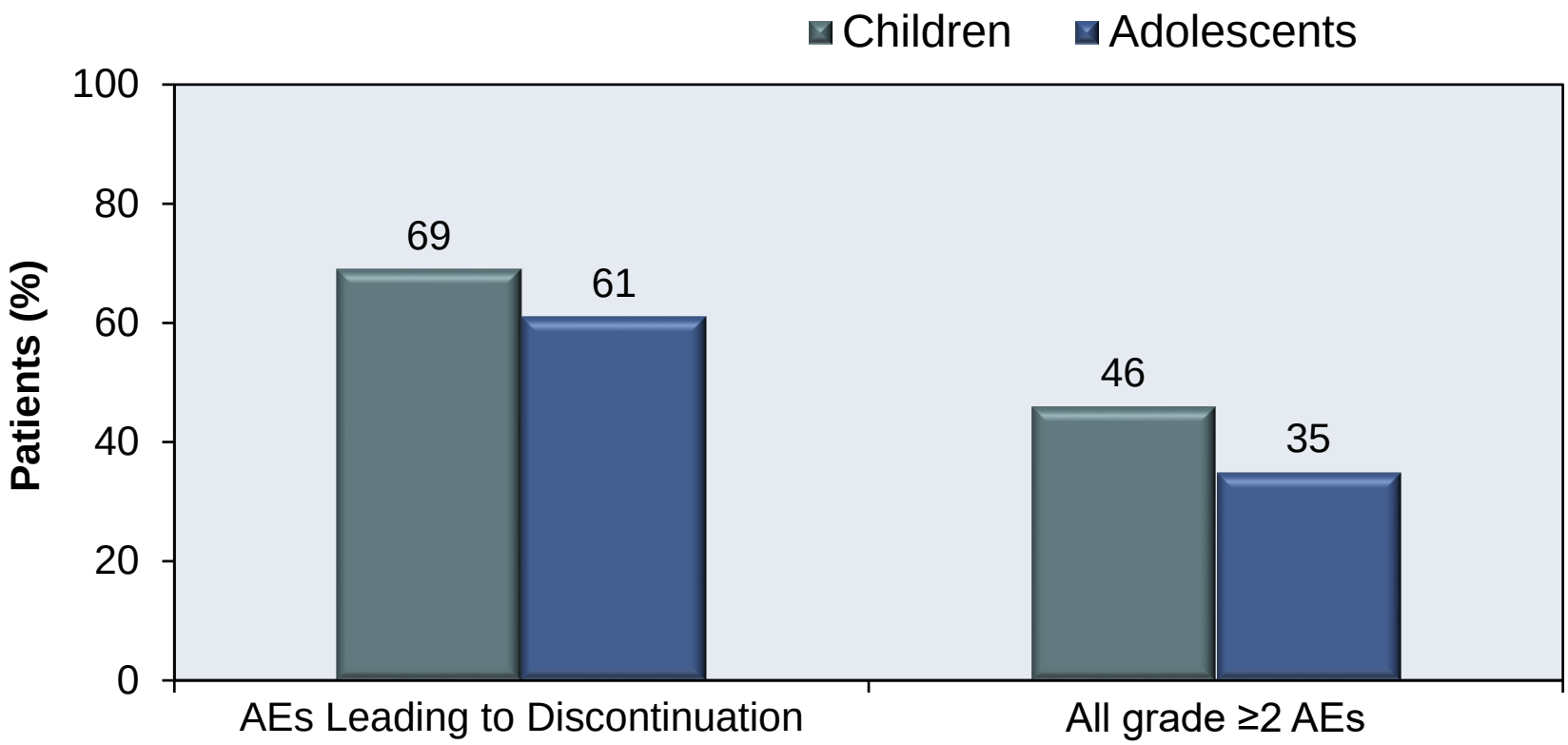


Source: Tudor-Williams G, et al. HIV Med. 2014;15:513-24.

Etravirine in Treatment-Experienced Children & Adolescents

PIANO: Result

Week 48: Adverse Events



Source: Tudor-Williams G, et al. HIV Med. 2014;15:513-24.

Etravirine in Treatment-Experienced Children & Adolescents
PIANO: Conclusions

Conclusions: “Results with etravirine 5.2 mg/kg bid (with OBR) in this treatment-experienced paediatric population and etravirine 200 mg bid in treatment-experienced adults were comparable. Etravirine is an NNRTI option for treatment-experienced paediatric patients.”

Source: Tudor-Williams G, et al. HIV Med. 2014;15:513-24.

SWITCH STUDIES

Etravirine

Etravirine plus Darunavir/r as Dual Therapy

INROADS Trial

Etravirine + Darunavir/r as Dual Therapy
INROADS: Design

Study Design: INROADS

- **Background**: Phase 2b, single-arm trial evaluating etravirine with darunavir plus ritonavir in treatment-experienced subjects or treatment-naïve persons with HIV and with transmitted drug-resistant HIV
- **Inclusion Criteria (n = 54)**
  - Age ≥18 years
  - Treatment-naïve: resistance to either efavirenz or nevirapine, but no resistance to etravirine darunavir
  - Treatment-experienced subjects
  - HIV RNA >500 copies/mL
  - CD4 count ≥50 cells/mm^3
- **Treatment Arms (all taken once daily)**
  - Etravirine 400 mg + Darunavir 800 mg + RTV 100 mg

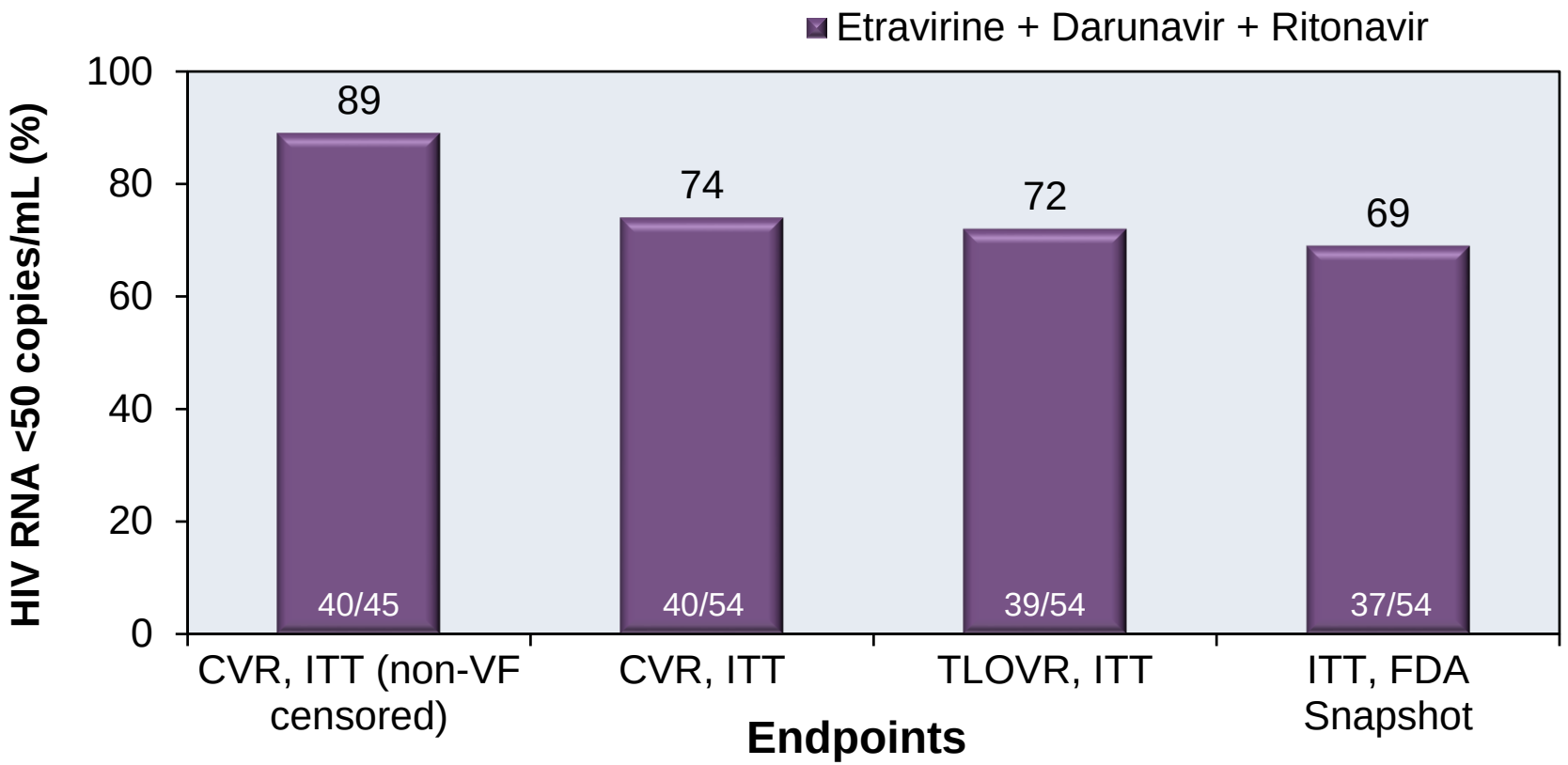
→ **Etravirine + Darunavir + Ritonavir** (n = 54)

* INROADS = **I**ntelence a**N**d p**R**ezista **O**nce **A** **D**ay **S**tudy

Source: Ruane PJ, et al. HIV Med. 2015;16:288-96.

Etravirine + Darunavir/r as Dual Therapy
INROADS: Result

Week 48: Virologic Response



CVR = confirmed virologic response; TLOVR = Time to loss of virologic; ITT: Intent-to-Treat.
CVR allows patients who are resuppressed after failure to be counted as virologic responders.

Source: Ruane PJ, et al. HIV Med. 2015;16:288-96.

Etravirine + Darunavir/r as Dual Therapy
INROADS: Conclusions

Conclusions: “Etravirine 400 mg and darunavir/ritonavir 800/100 mg as a two-drug once-daily regimen in treatment-experienced subjects or treatment-naïve subjects with transmitted resistance was virologically efficacious and well tolerated.”

Source: Ruane PJ, et al. HIV Med. 2015;16:288-96.

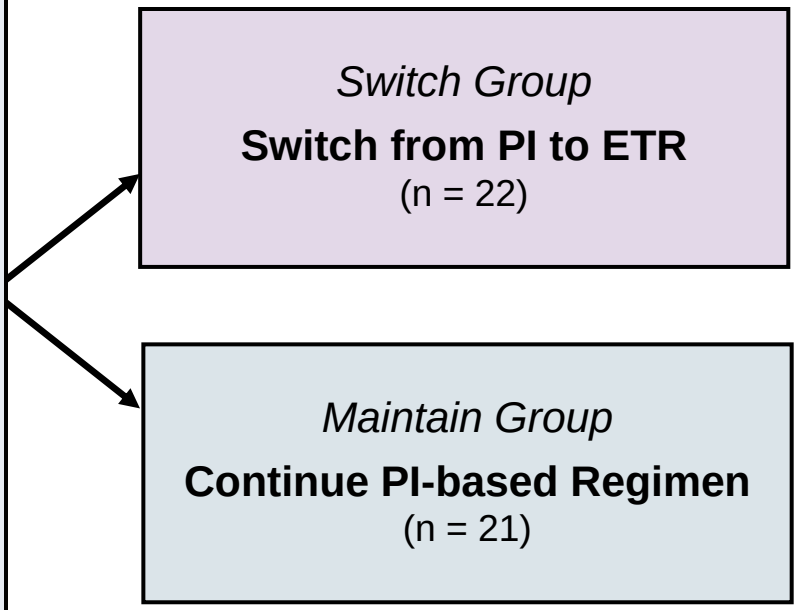
Switch to Etravirine from PI-Based Regimen

ETRA-SWITCH STUDY

Switch to Etravirine from PI-Based Regimen
ETRA-SWITCH: Design

Study Design: ETRA-SWITCH

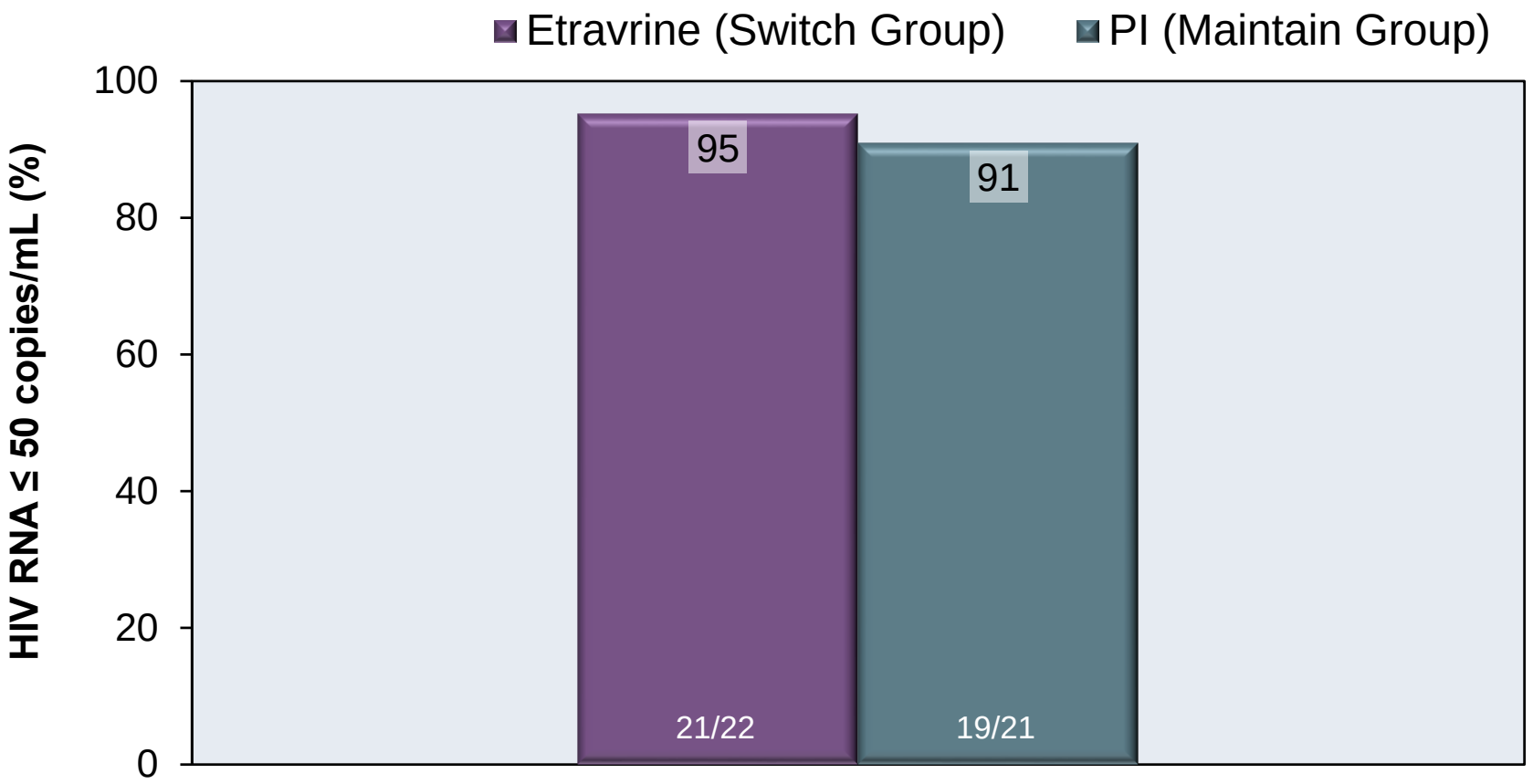
- **Background**: Open label, randomized phase 3b trial that enrolled persons with HIV who had suppressed HIV RNA levels while taking a ritonavir-boosted PI plus 2NRTIs and examined the efficacy and safety of switching the ritonavir-boosted PI to etravirine
- **Inclusion Criteria (n = 43)**
  - On PI >12 months
  - HIV RNA <50 copies/mL for >6 months
  - No NRTI or NNRTI resistance
  - No prior virologic failure with prior regimen
  - Patients had dyslipidemia OR use of lipid lowering medication OR GI disturbance OR persistent dissatisfaction with current regimen
- **Treatment Arms**
  - Switch PI in regimen to etravirine 400 mg/day
  - Continue current PI-based ART regimen



Source: Echeverría P, et al. PLoS One. 2014;9:e84676.

Switch to Etravirine from PI-Based Regimen
ETRA-SWITCH: Result

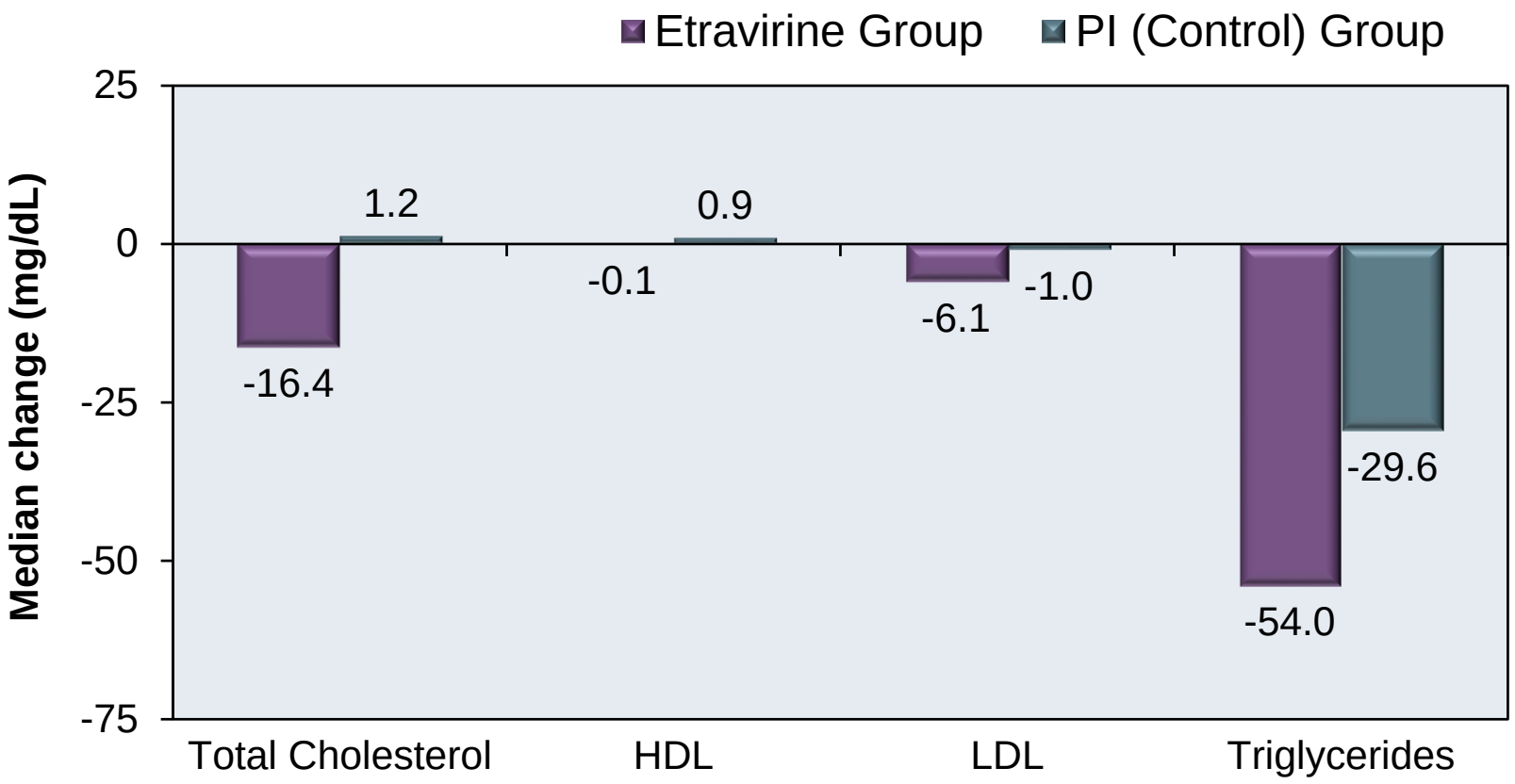
Week 48: Virologic Response (ITT Analysis, Missing = Failure)



Source: Echeverría P, et al. PLoS One. 2014;9:e84676.

Switch to Etravirine from PI-Based Regimen
ETRA-SWITCH: Result

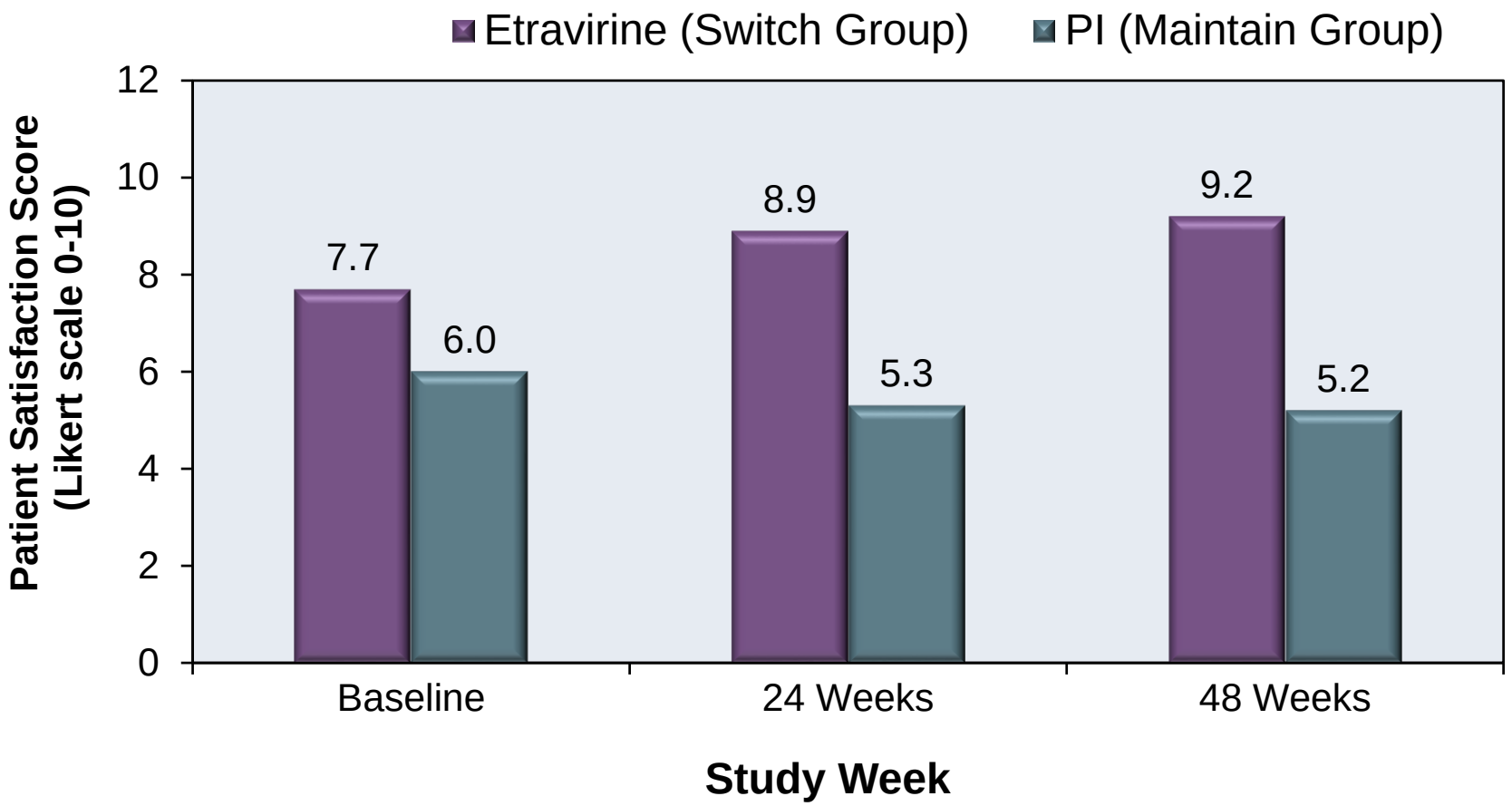
Week 48: Change in Plasma Lipids from Baseline



Source: Echeverría P, et al. PLoS One. 2014;9:e84676.

Switch to Etravirine from PI-Based Regimen
ETRA-SWITCH: Result

Patient Satisfaction Scores



Source: Echeverría P, et al. PLoS One. 2014;9:e84676.

Switch to Etravirine from PI-Based Regimen
ETRA-SWITCH: Conclusions

Conclusion: “Switch from a PI-based regimen to a once-daily combination based on ETR maintained undetectable VL during 48 weeks in virologically suppressed HIV-infected patients while lipid profile and patient satisfaction improved significantly.”

Source: Echeverría P, et al. PLoS One. 2014;9:e84676.

Switch to Etravirine from Efavirenz

SWITCH-EE STUDY

Switch from Efavirenz to Etravirine
SWITCH-EE: Design

Study Design: SWITCH-EE

- **Background**: Randomized, double-blind, crossover study comparing the safety and efficacy of etravirine with efavirenz
- **Inclusion Criteria (n = 58)**
  - Age ≥18 years
  - On EFV-containing ART regimen for ≥3 months
  - HIV RNA <50 copies/mL for ≥3 months
- **Treatment Arms**
  - EFV 600 mg daily + NRTI backbone x 6 weeks, then switch EFV to ETR
  - ETR 400 mg daily + NRTI backbone x 6 weeks, then switch ETR to EFV

"EFV First" Group

EFV 600 mg QD + NRTIs, then switch EFV to ETR

(n = 28)

"ETR First" Group

ETR 400 mg QD + NRTIs, then switch ETR to EFV

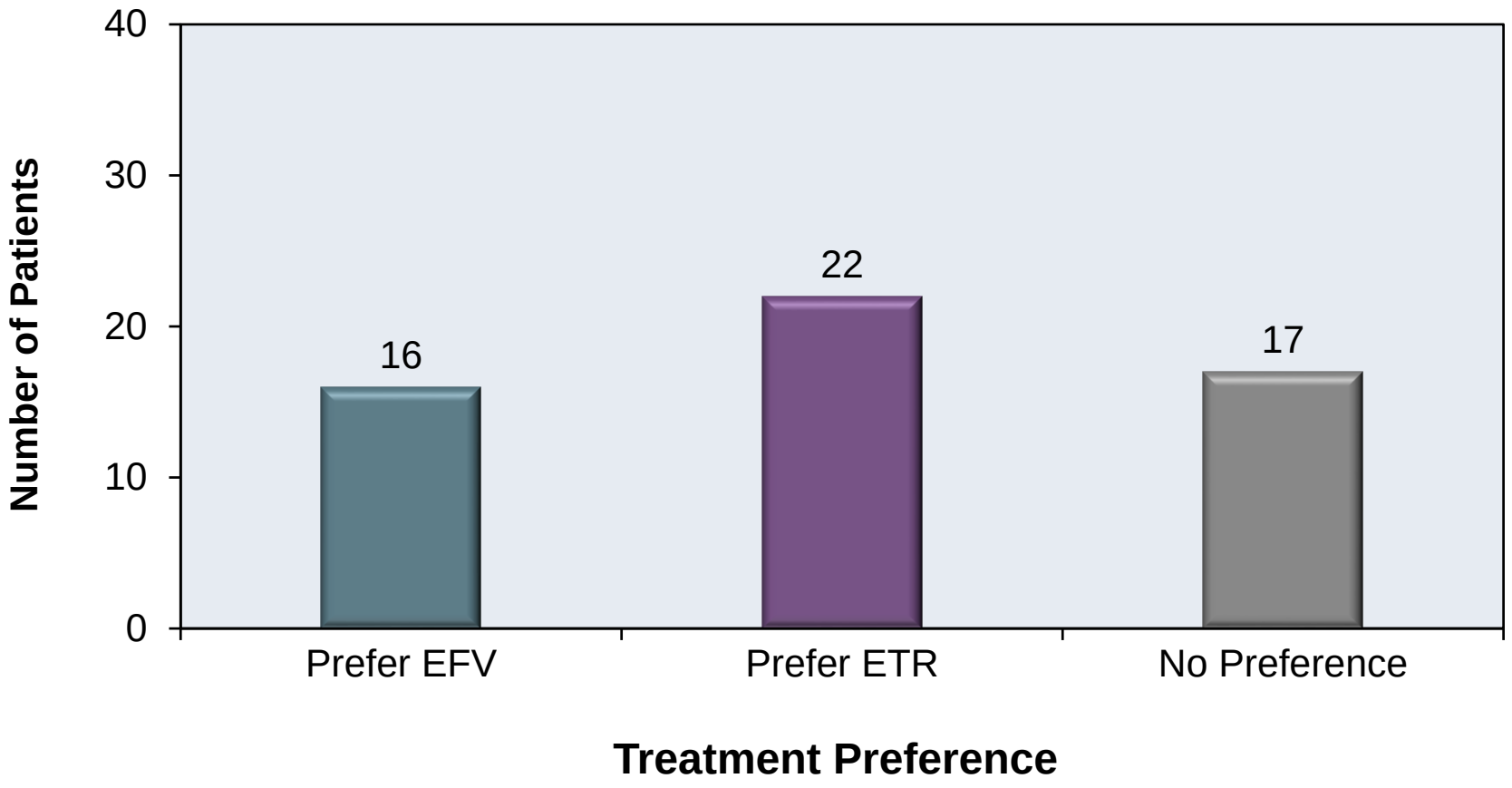
(n = 30)

Source: Nyugen A, et al. AIDS. 2011;25:57-63.

Switch from Efavirenz to Etravirine

SWITCH-EE: Result

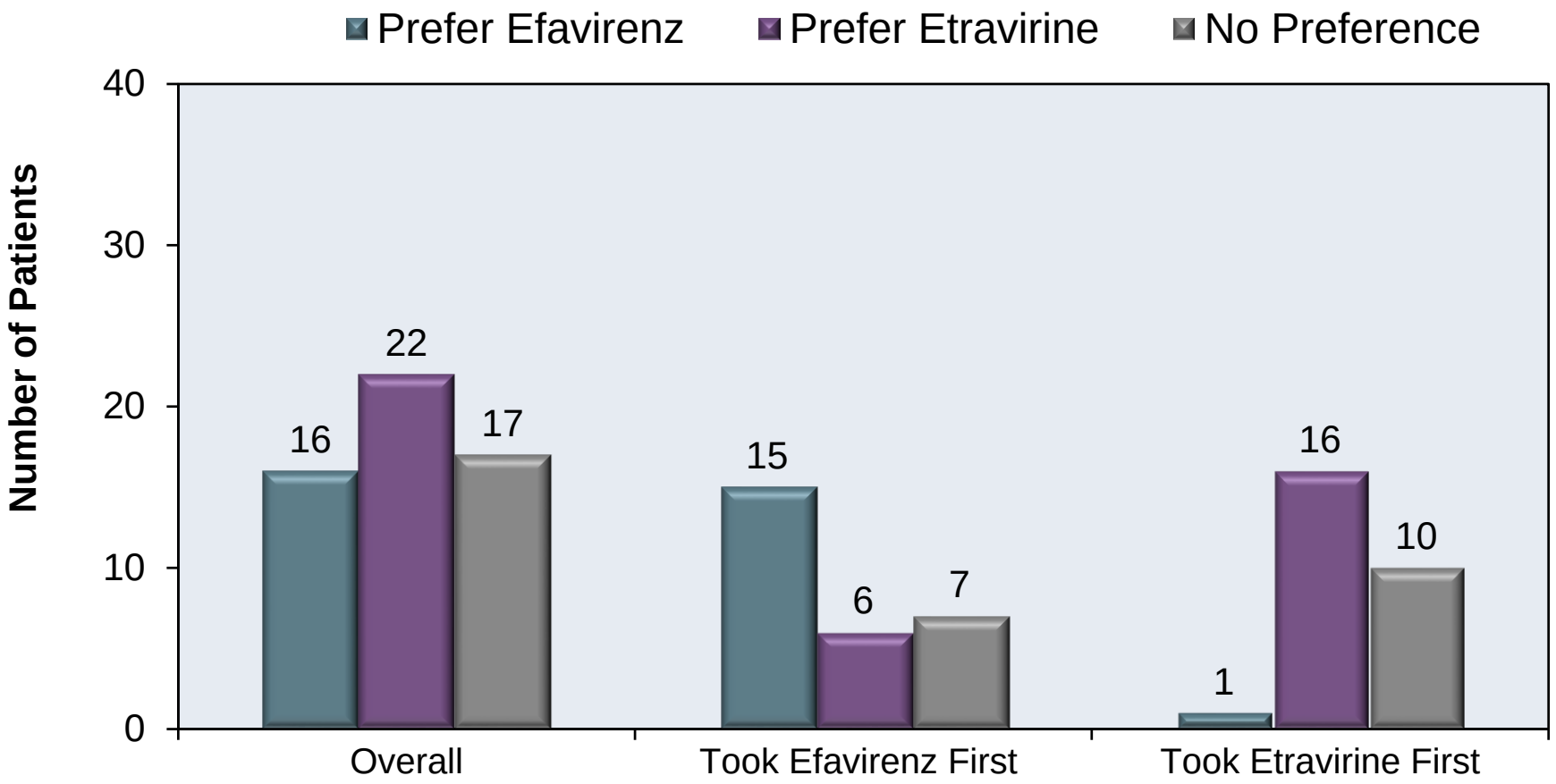
Week 12: Treatment Preference



Source: Nyugen A, et al. AIDS. 2011;25:57-63.

Switch from Efavirenz to Etravirine
SWITCH-EE: Result

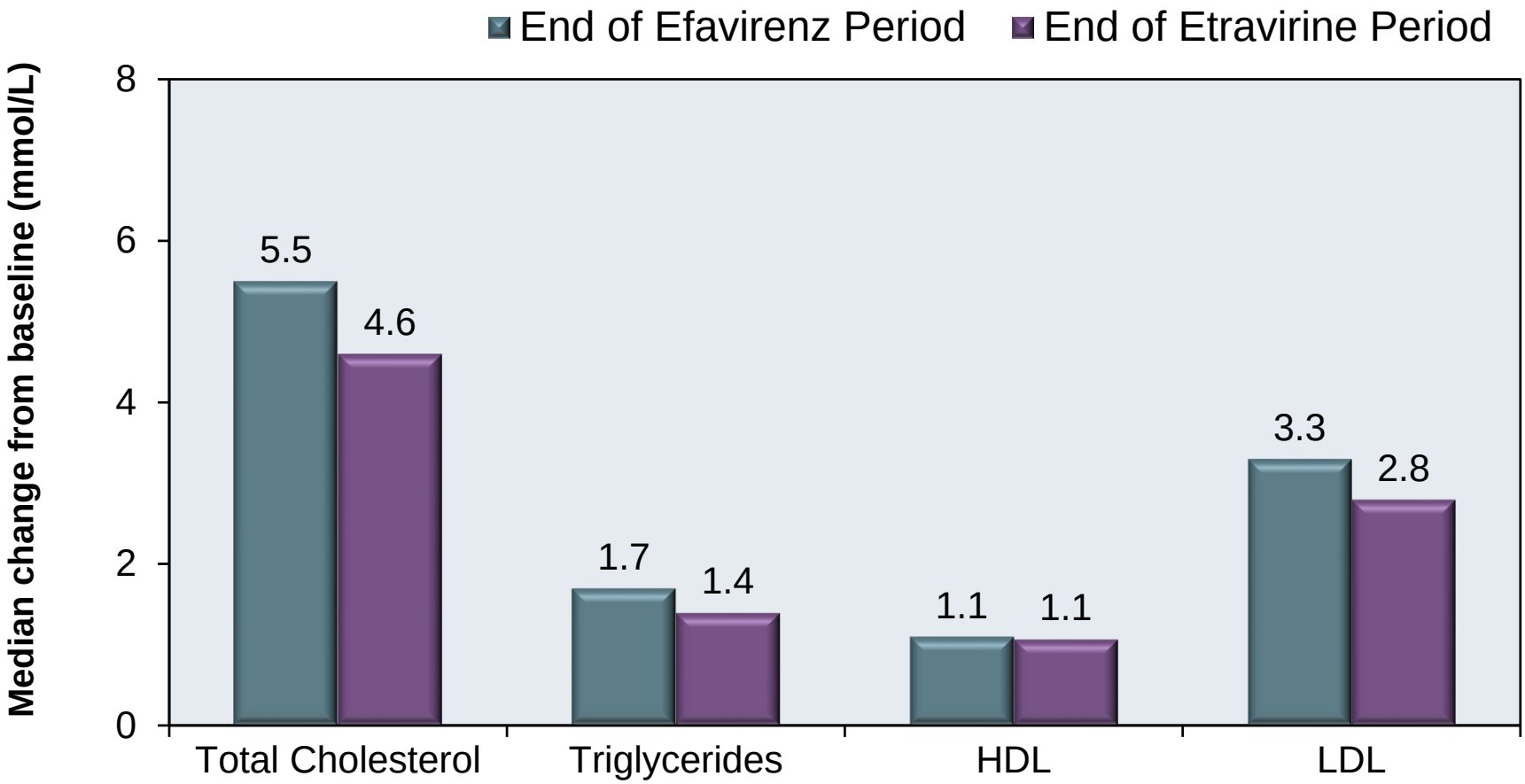
Week 12: Treatment Preference, with Significant Order Effect



Source: Nyugen A, et al. AIDS. 2011;25:57-63.

Switch from Efavirenz to Etravirine
SWITCH-EE: Result

Week 12: Change in Plasma Lipids from Baseline



Source: Nyugen A, et al. AIDS. 2011;25:57-63.

Switch from Efavirenz to Etravirine
SWITCH-EE: Conclusions

Conclusion: “After substitution of efavirenz by etravirine, patients did not express a significant preference for etravirine. There was no measurable effect on neuropsychiatric symptoms and sleep. Cholesterol decreased.”

Source: Nyugen A, et al. AIDS. 2011;25:57-63.

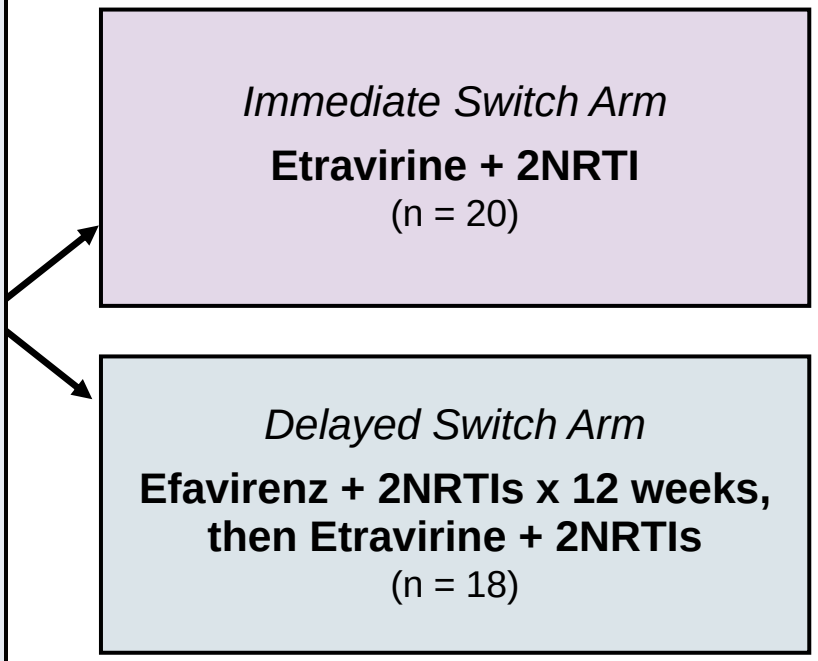
Switch to Etravirine from Efavirenz due to CNS Toxicity

SSAT-029 STUDY

Switch to Etravirine from Efavirenz Due to CNS Toxicity
SSAT-029: Design

Study Design: SSAT-029

- **Background**: Randomized, double-blind, phase IV trial evaluating the impact of switching from etravirine to efavirenz on central nervous system (CNS) symptoms on a stable, fully suppressive efavirenz-based regimen
- **Inclusion Criteria (n = 38)**
  - On efavirenz plus 2NRTIs >12 weeks
  - Ongoing CNS symptoms
  - HIV RNA <50 copies/mL
  - CD4 count >50 cells/mm^3
  - No previous exposure to etravirine or rilpivirine
- **Treatment Arms**
  - ETR + EFV-placebo + 2NRTI x 12 weeks, then open-label ETR + 2NRTIs
  - EFV + ETR-placebo + 2NRTI x 12 weeks, then switch to open-label ETR + 2NRTIs

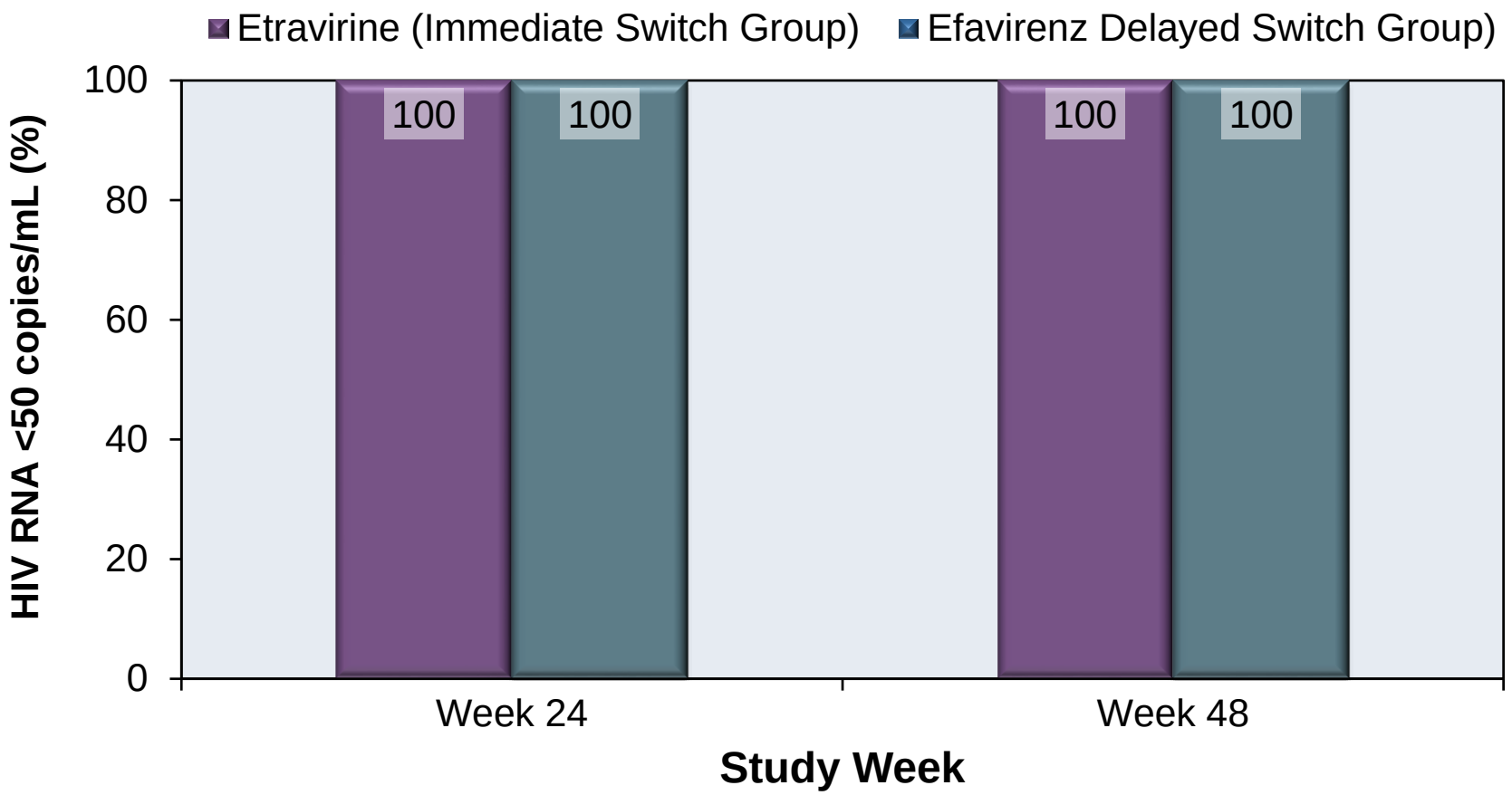


Source: Waters L, et al. AIDS. 2011;25:65-71.

Switch to Etravirine from Efavirenz Due to CNS Toxicity

SSAT-029: Result

Week 24 and 48: Virologic Response (on-treatment analysis)

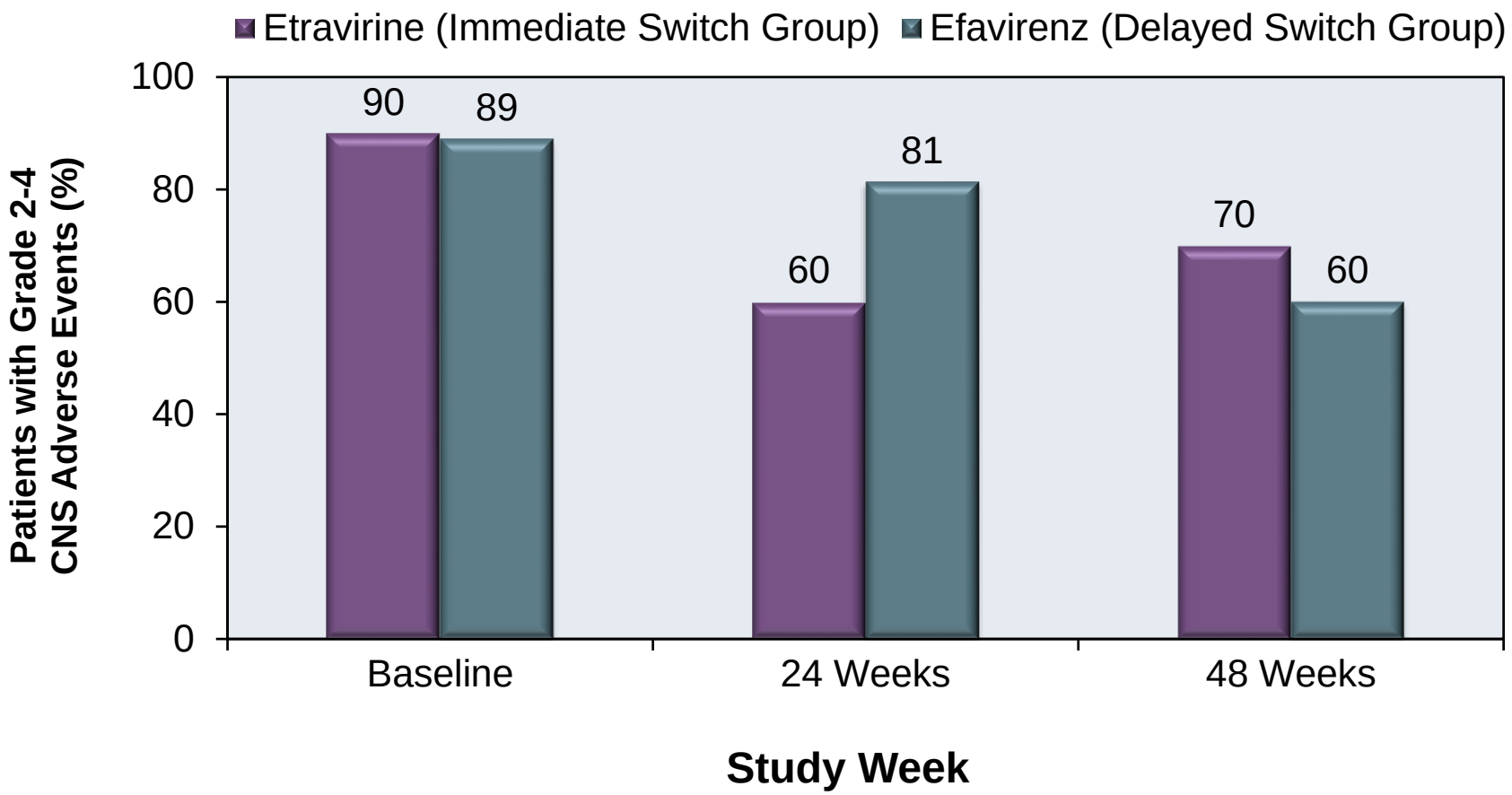


Source: Waters L, et al. AIDS. 2011;25:65-71.

Switch to Etravirine from Efavirenz Due to CNS Toxicity

SSAT-029: Result

Change in CNS Adverse Events, by Study Group

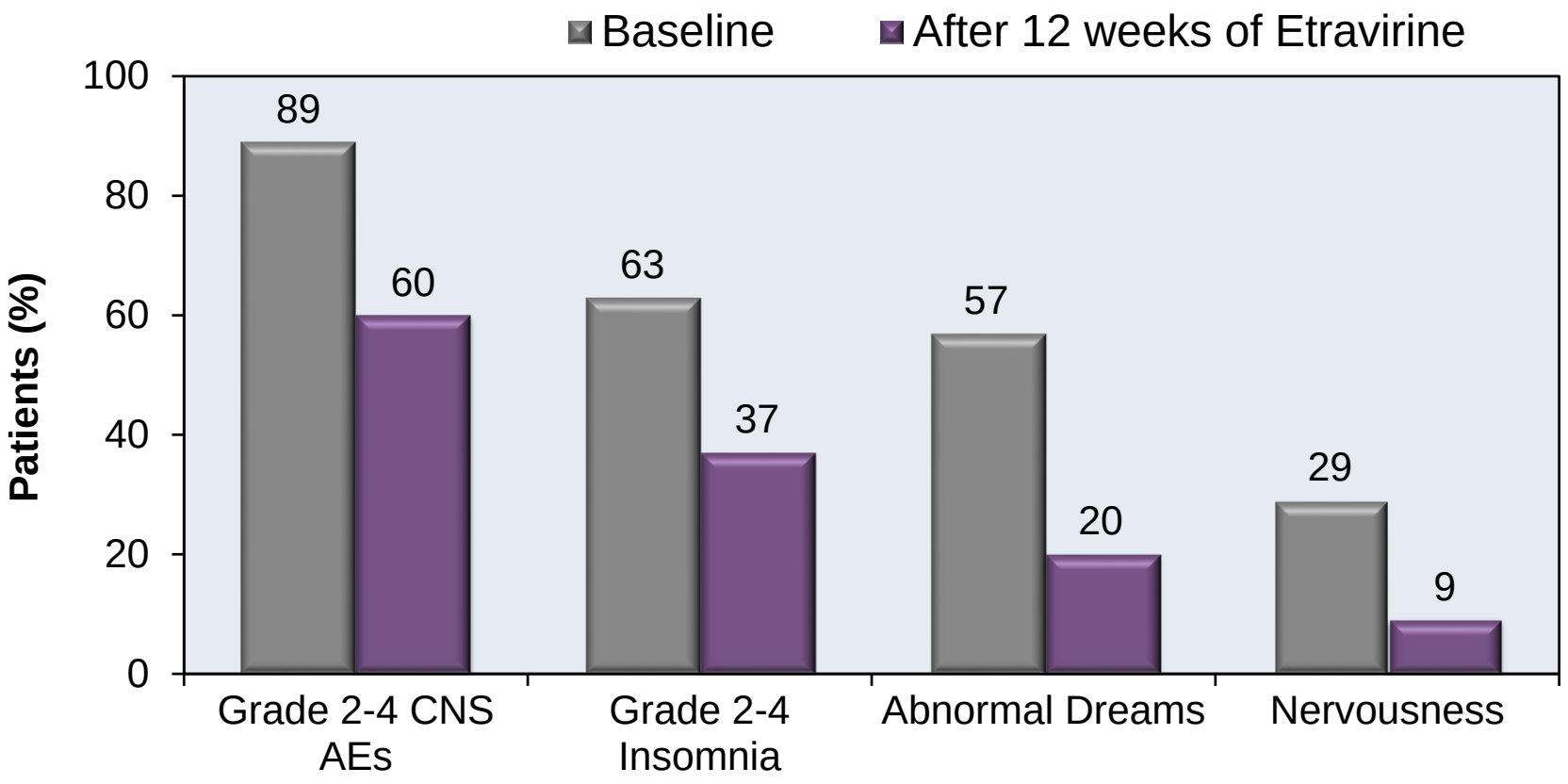


Source: Waters L, et al. AIDS. 2011;25:65-71.

Switch to Etravirine from Efavirenz Due to CNS Toxicity

SSAT-029: Result

Change in CNS Adverse Events: Combined Analyses

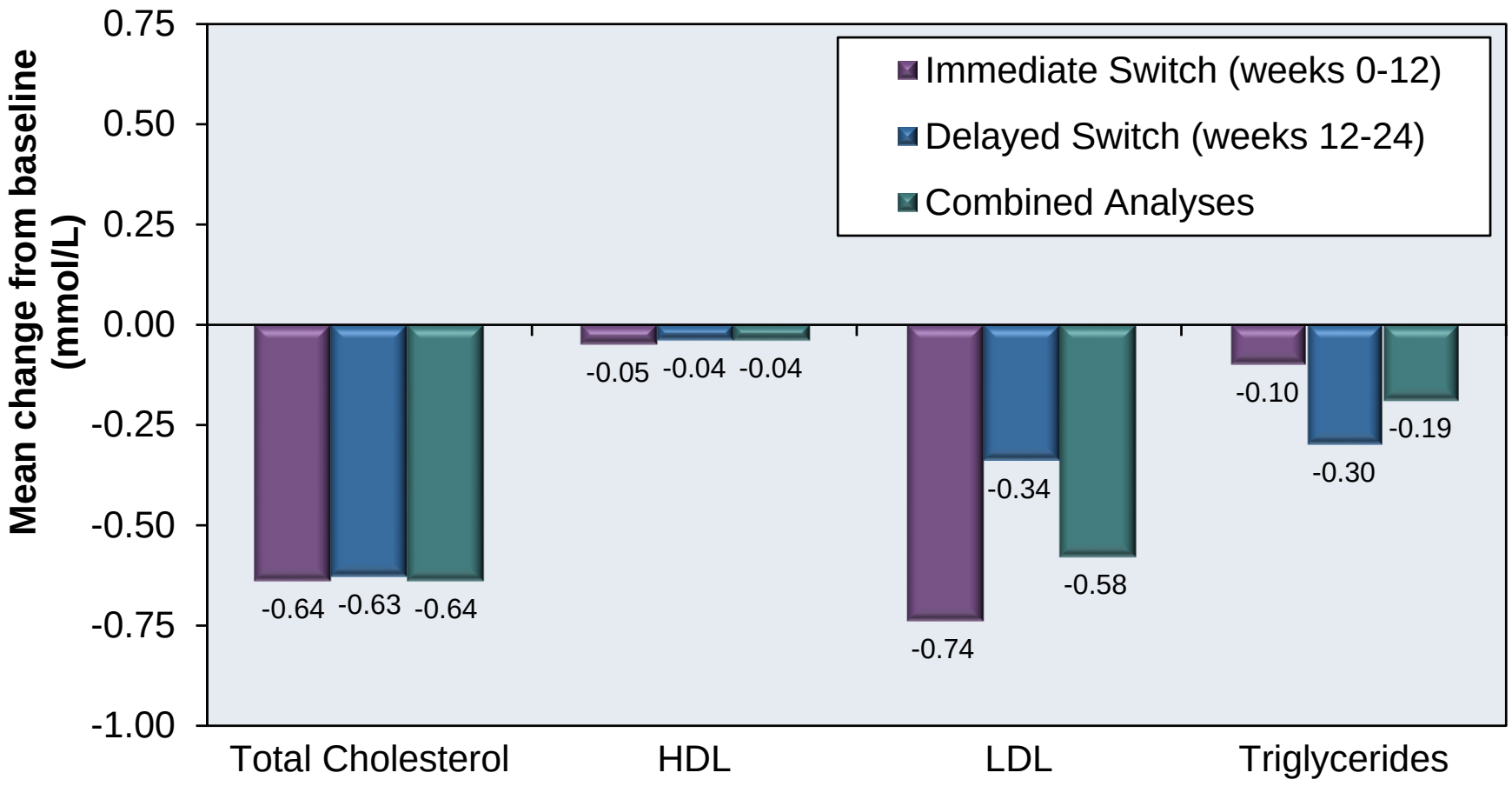


Source: Waters L, et al. AIDS. 2011;25:65-71.

Switch to Etravirine from Efavirenz Due to CNS Toxicity

SSAT-029: Result

Lipid Changes After 12 Weeks of Etravirine



Source: Waters L, et al. AIDS. 2011;25:65-71.

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Switch from Efavirenz to Etravirine
SSAT-029: Conclusions

Conclusion: “Switching efavirenz to etravirine led to a significant reduction in overall grade 2-4 CNS adverse events, including insomnia, abnormal dreams and nervousness as individual adverse event. Lack of improvement for some events suggests other causative factors.”

Source: Waters L, et al. AIDS. 2011;25:65-71.

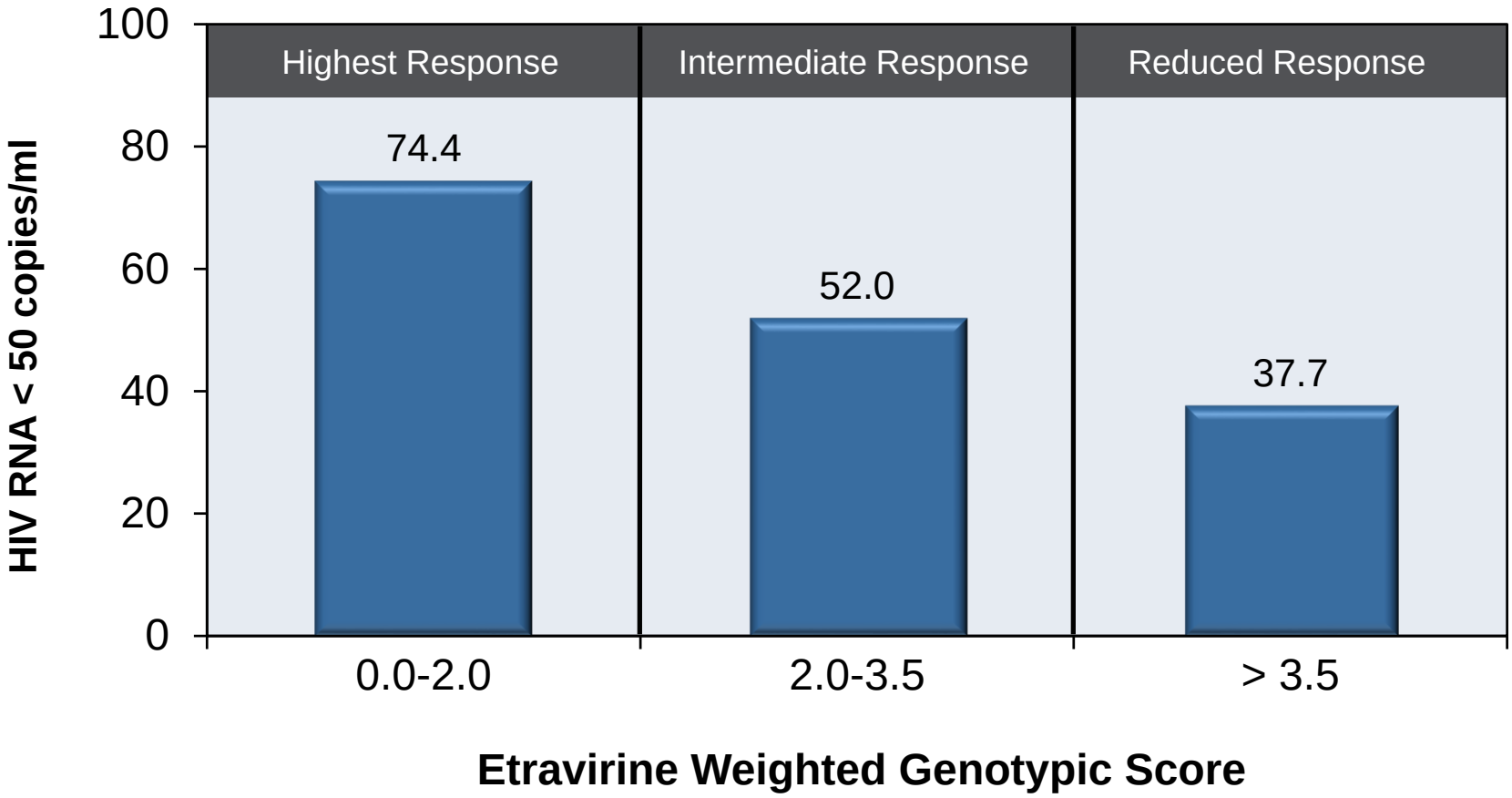
Weighted Scores for Etravirine-Associated Mutations Based on Data from Duet 1 & 2

Etravirine Resistance-Associated Mutations and Response to Etravirine	
Etravirine Mutation Score	**Predicted Response Rate**
0 – 2.0	Highest response rate
2.5 - 3.5	Intermediate response
>3.5	Progressive reduced response

Source: Vingerhoets J, et al. AIDS. 2010;24:503-14.

Weighted Scores for Etravirine-Associated Mutations Based on Data from Duet 1 & 2

Virologic Response at Week 24 in Duet-1 and Duet-2



Source: Vingerhoets J, et al. AIDS. 2010;24:503-14.

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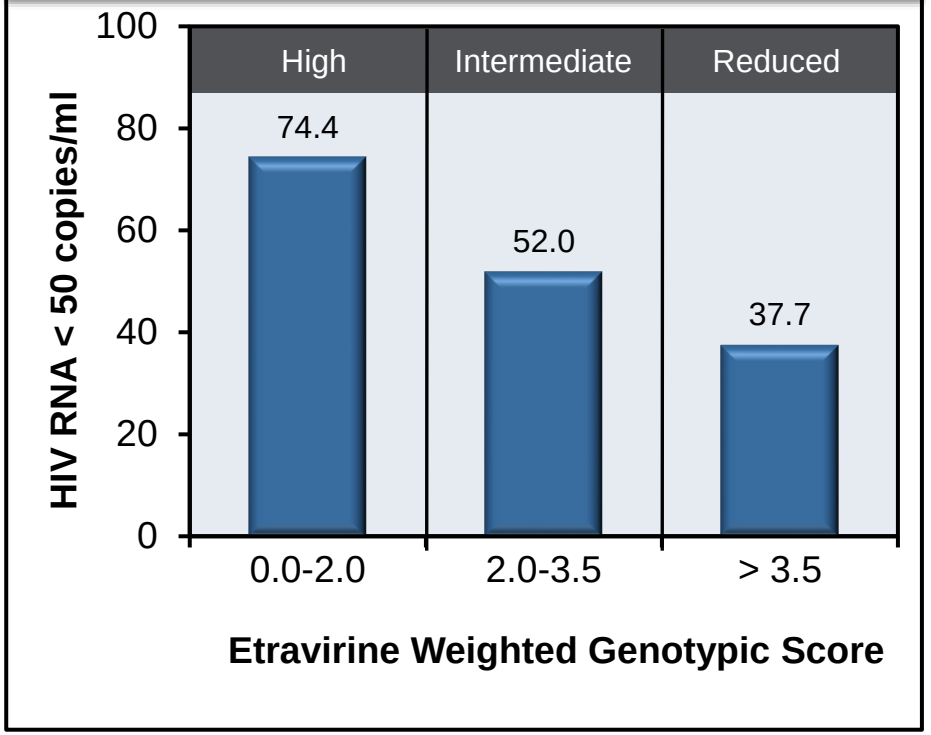
Baseline Etravirine Resistance-Associated Mutations Predicting Response to Etravirine; DUET 1 & 2

Individual Mutation Weight to Etravirine			
1.0	1.5	2.5	3
V90I	V106I	L100I	Y181I
A98G	E138A	K101P	Y181V
K101E	V179F	Y181C	
K101H	G190S	M230L	
V179D			
V179T			
G190A			

Virologic Response at Week 24 in Duet-1 & Duet-2



From: Vingerhoets J, et al. AIDS. 2010;24:503-14.

Weighted Scores for Etravirine-Associated Mutations Based on Monogram Biosciences Data

Individual Mutation Weight to Etravirine (n = 30 mutations)			
1	2	3	4
V90I	K101E	E138A	L100I
K101H	V106A	E138G	K101P
V106M	E138K	V179E	Y181C
E138Q	V179L	G190Q	Y181I
V179D	Y188L	M230L	
V179F		K238N	
V179M			
Y181F			
V189I			
G190E			
G190T			
H221Y	Score ≥ 4 = Reduced Susceptibility		
P225H			
K238T			

Source: Benhamida J, et al. XVII International HIV Drug Resistance Workshop. 2008. Abstract 130.

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Acknowledgment

The **National HIV Curriculum** is an AIDS Education and Training Center (AETC) Program supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $800,000 with 0% financed with non-governmental sources. This project is led by the University of Washington's Infectious Diseases Education and Assessment (IDEA) Program.

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AETC AIDS Education & Training Center Program