National HIV Curriculum

Maraviroc (*Selzentry*)

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AETC AIDS Education & Training Center Program

Maraviroc (*Selzentry*)

Selzentry
[sell-ZEN-tree]

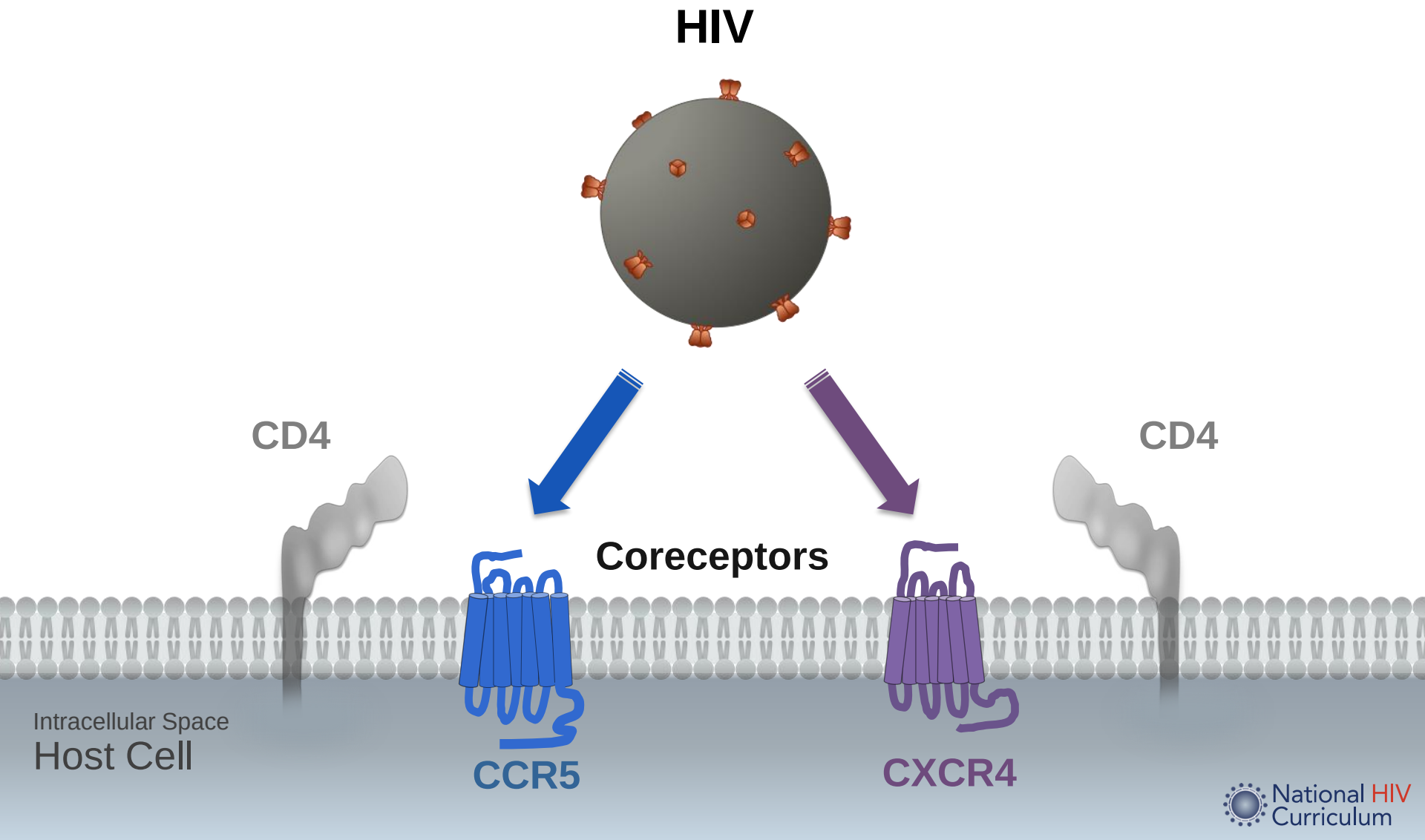
300 mg

150 mg

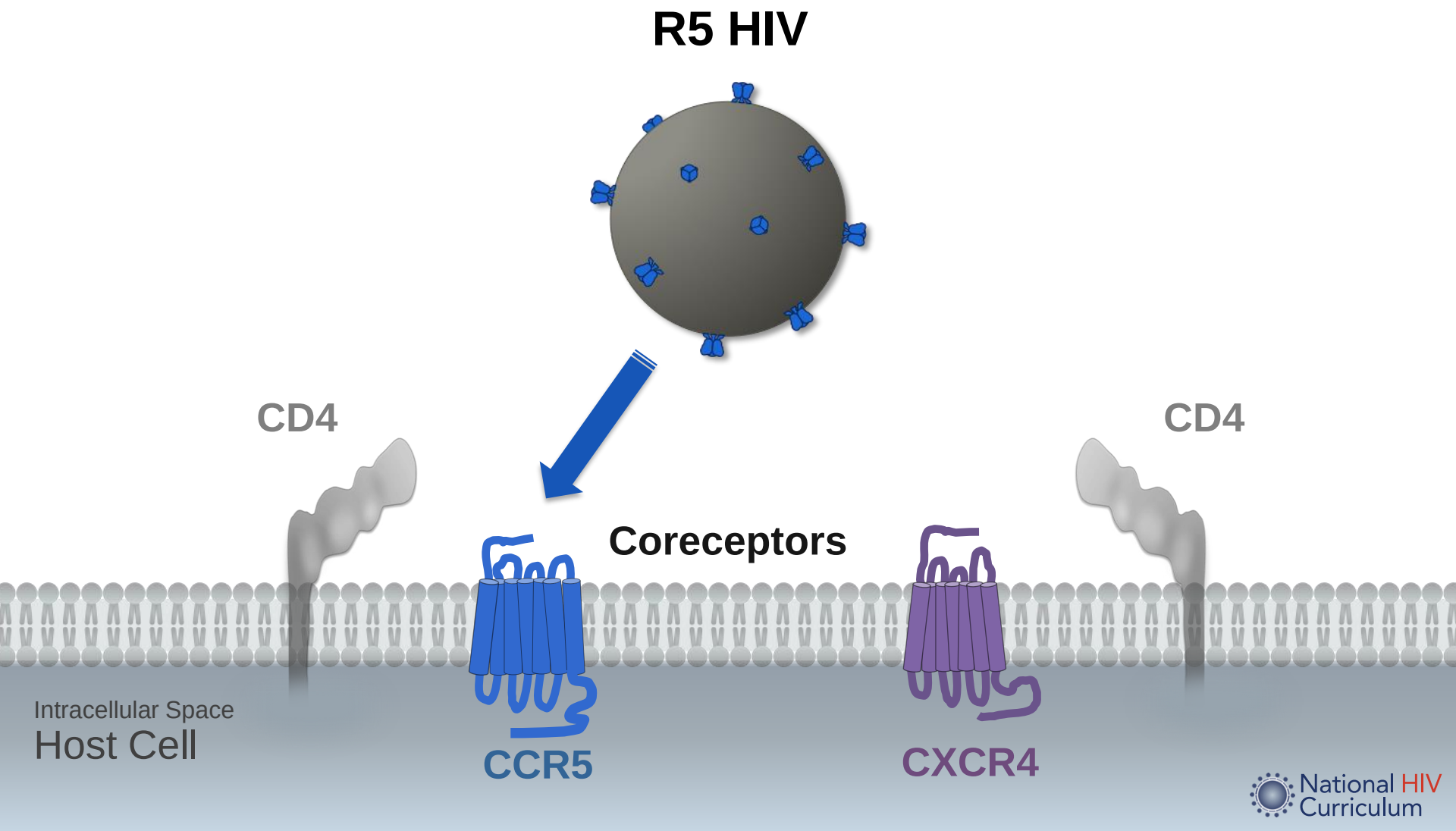
ANTIRETROVIRAL THERAPY

CCR5 Receptor Antagonists

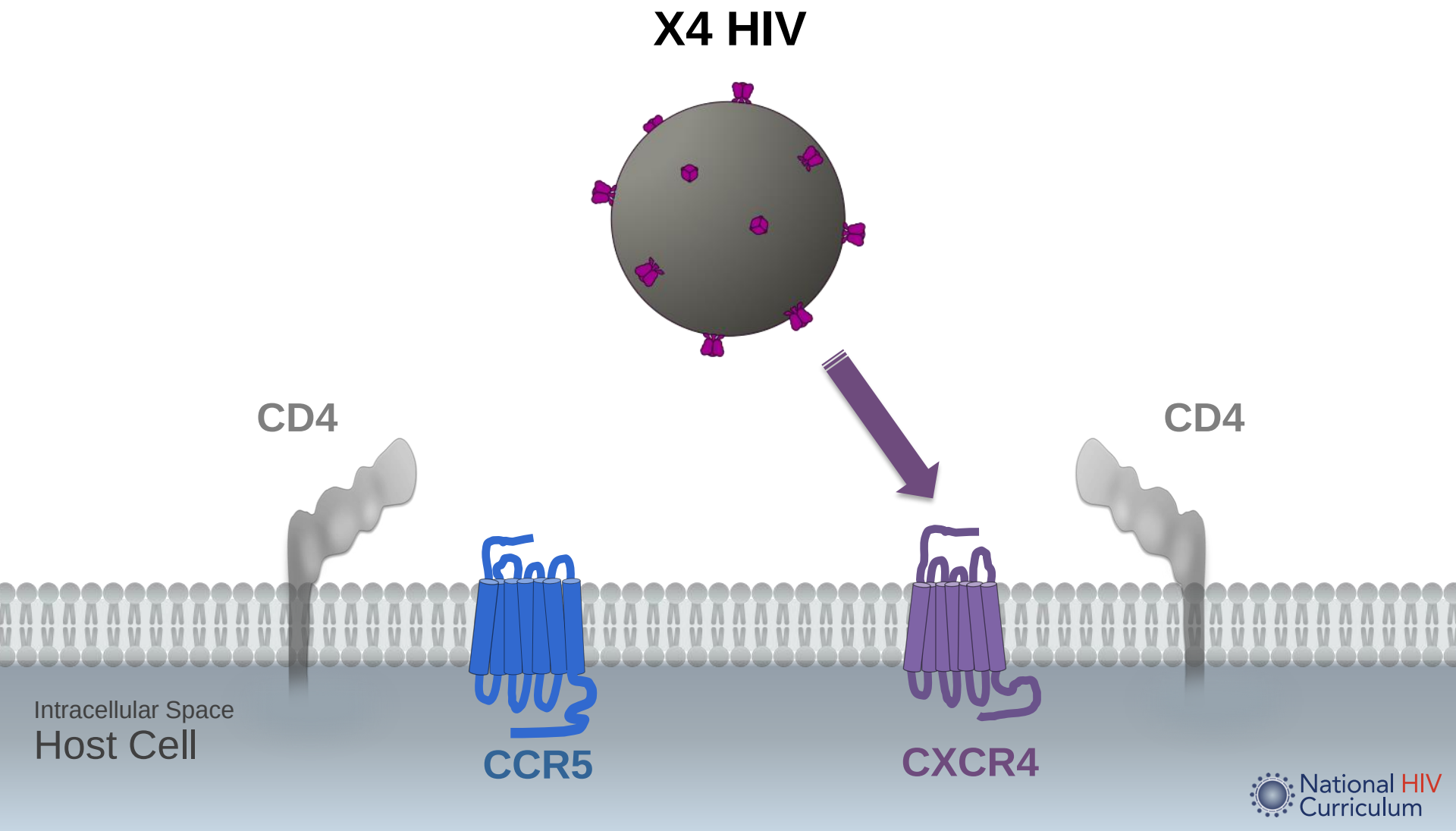
Host Cellular Receptors Involved in HIV Entry



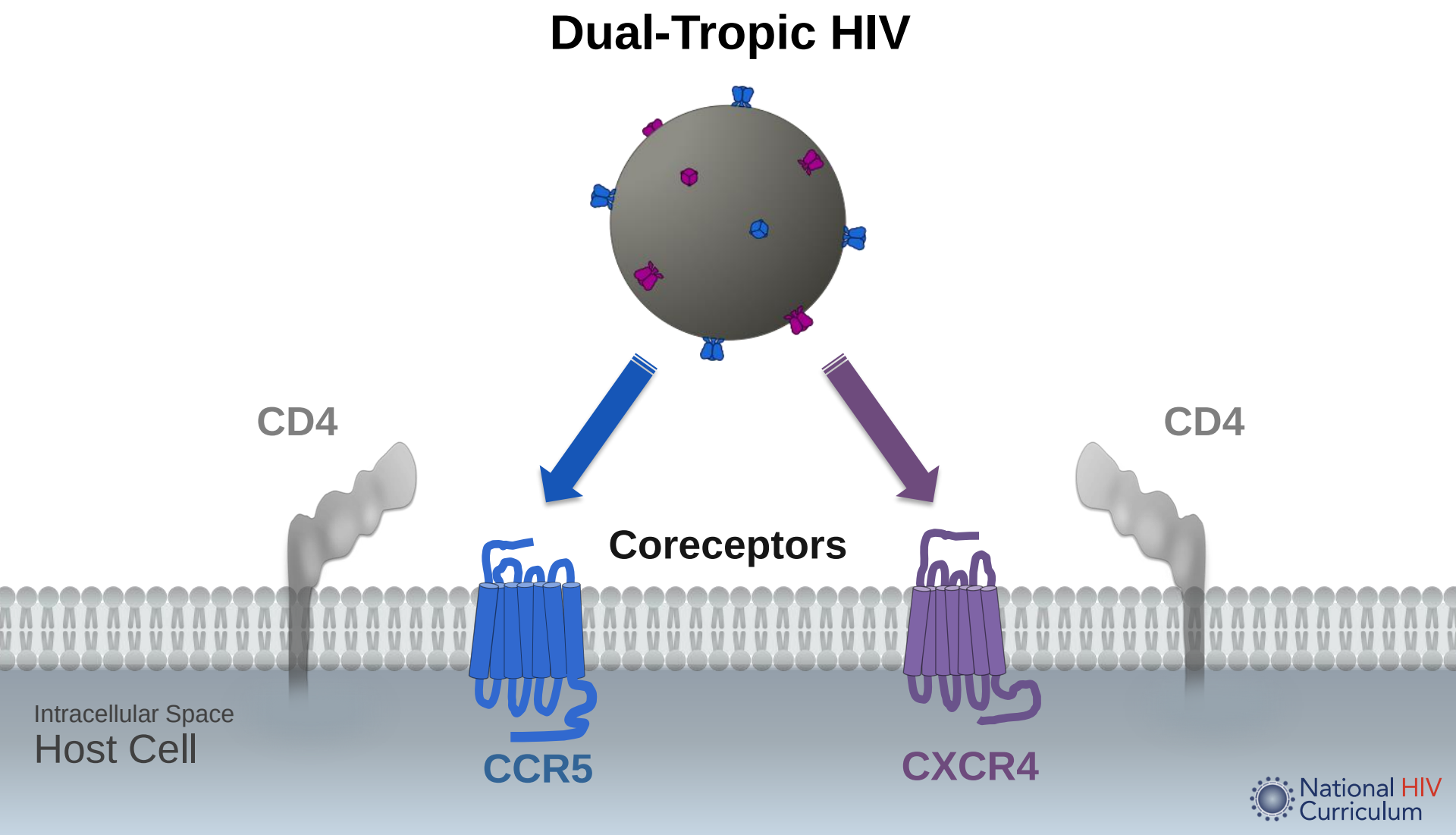
CCR5 Tropic (R5) HIV-1



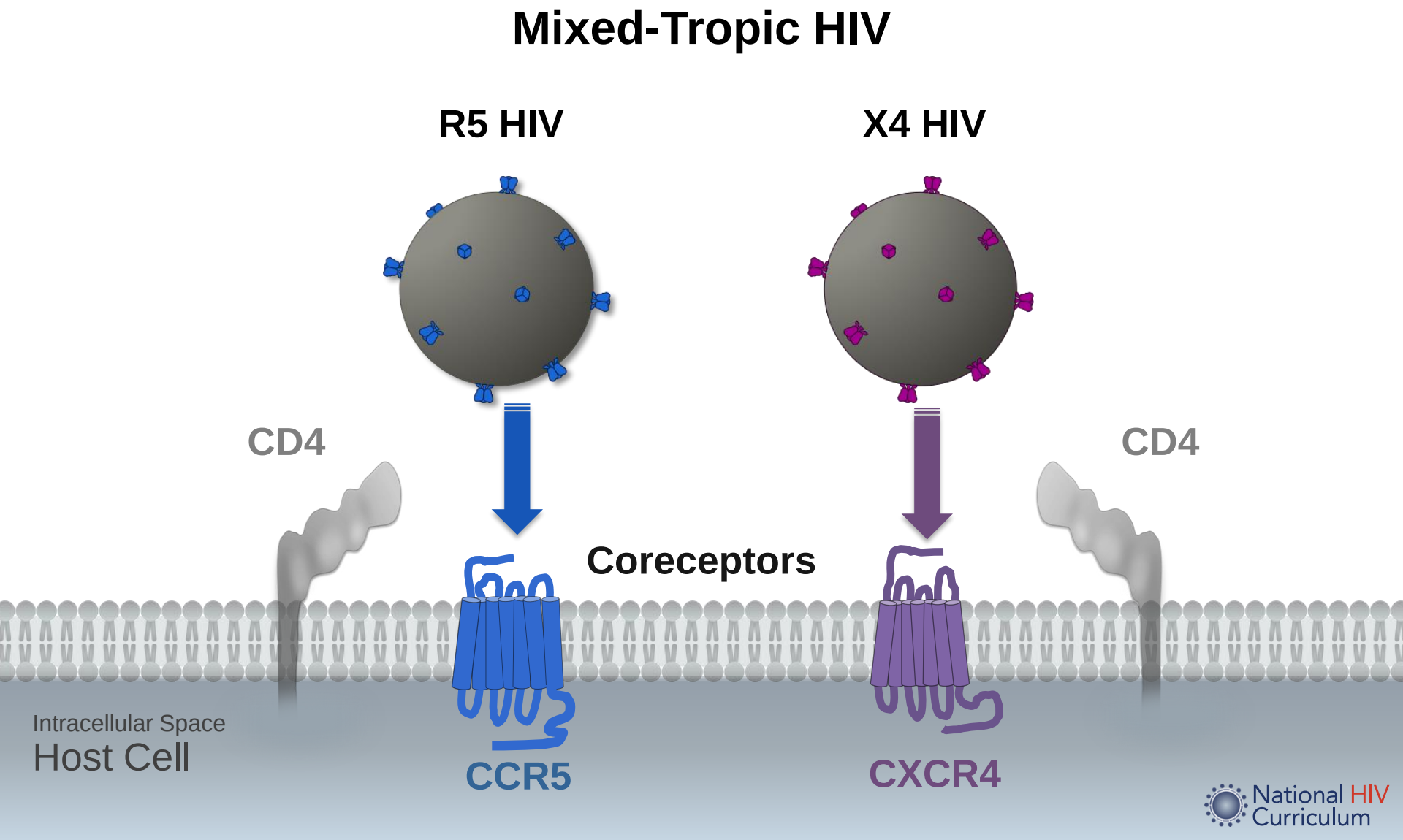
CXCR4 Tropic (X4) HIV-1



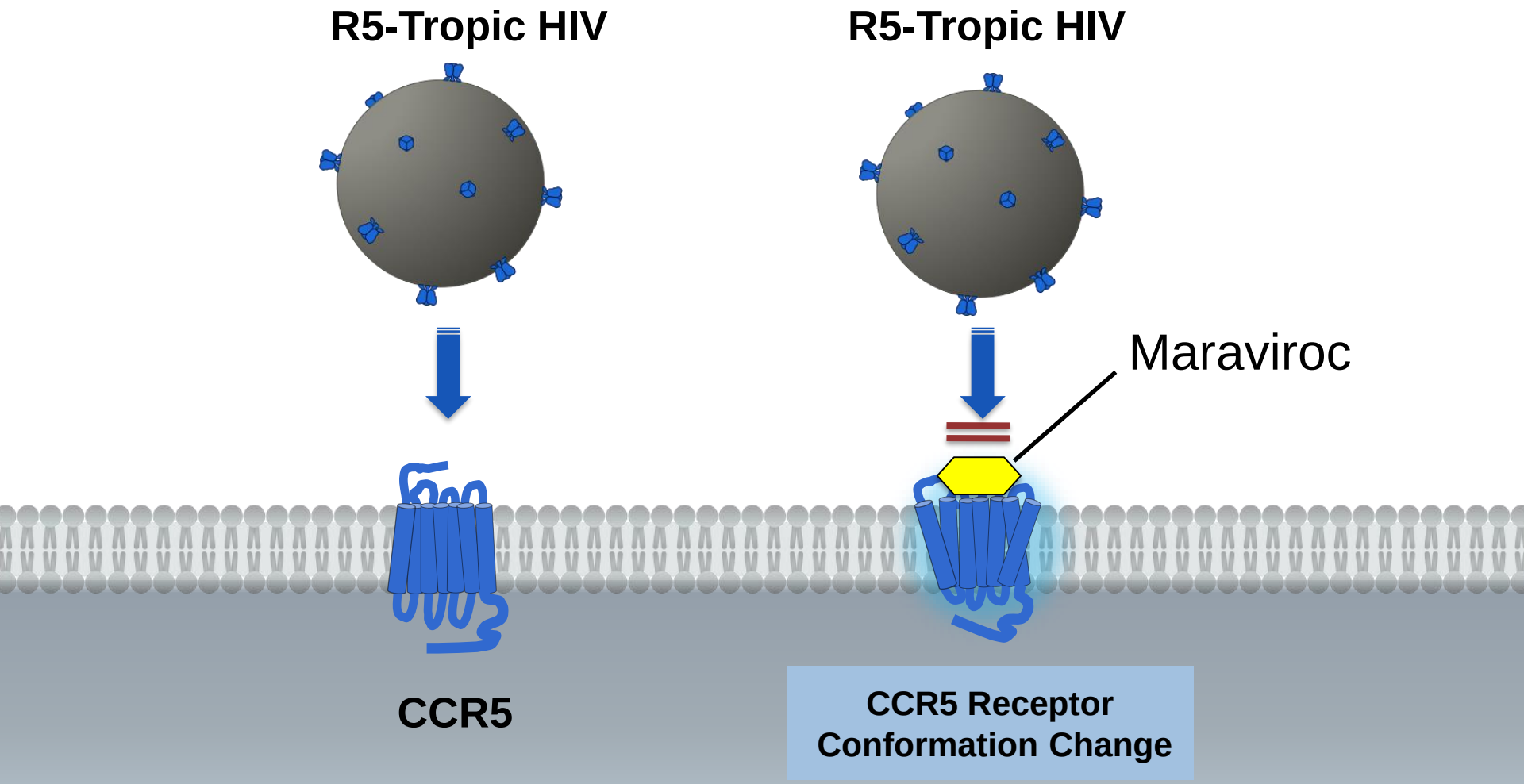
Dual Tropic HIV-1



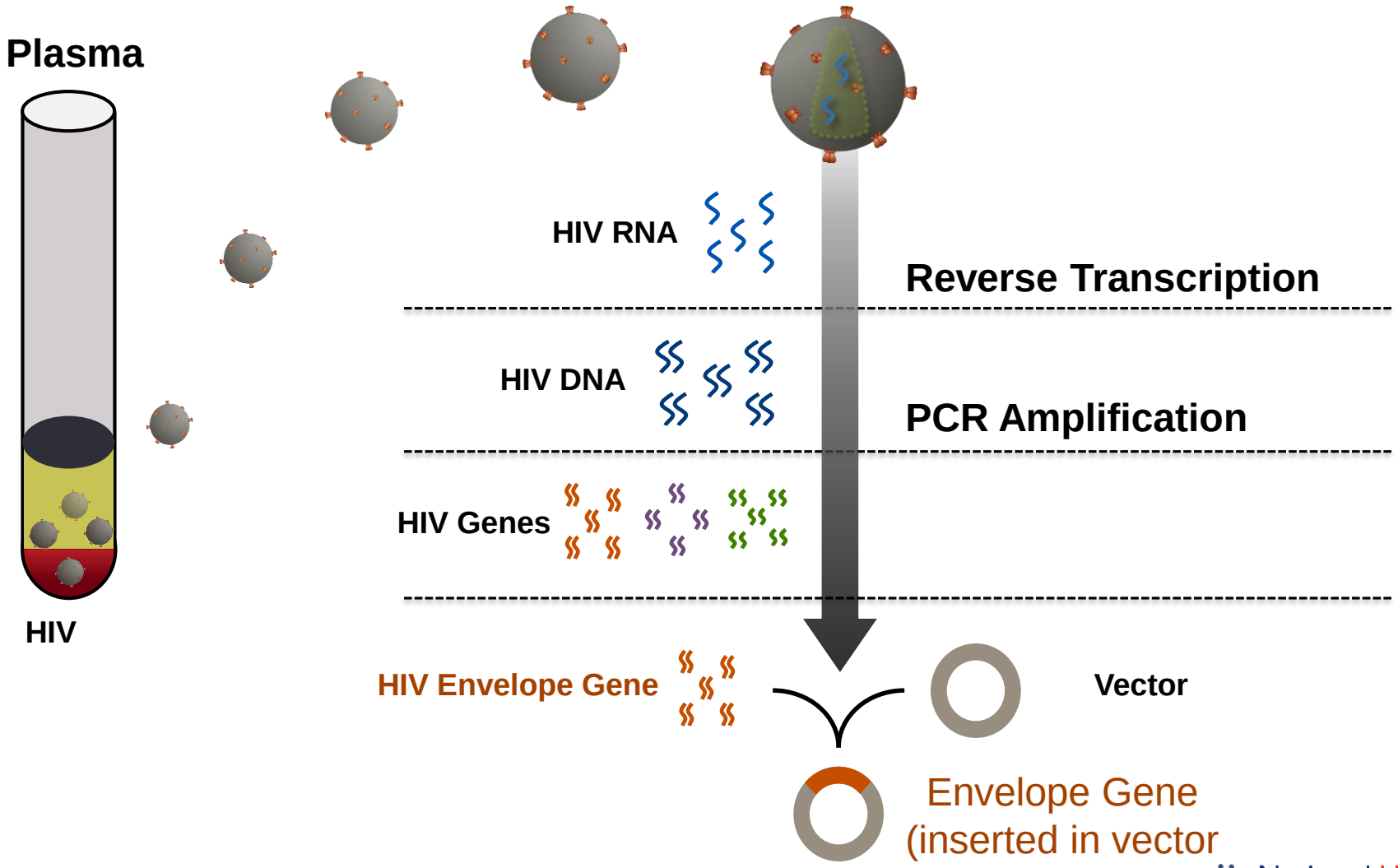
Mixed Tropic HIV-1



Maraviroc: Mechanism of Action

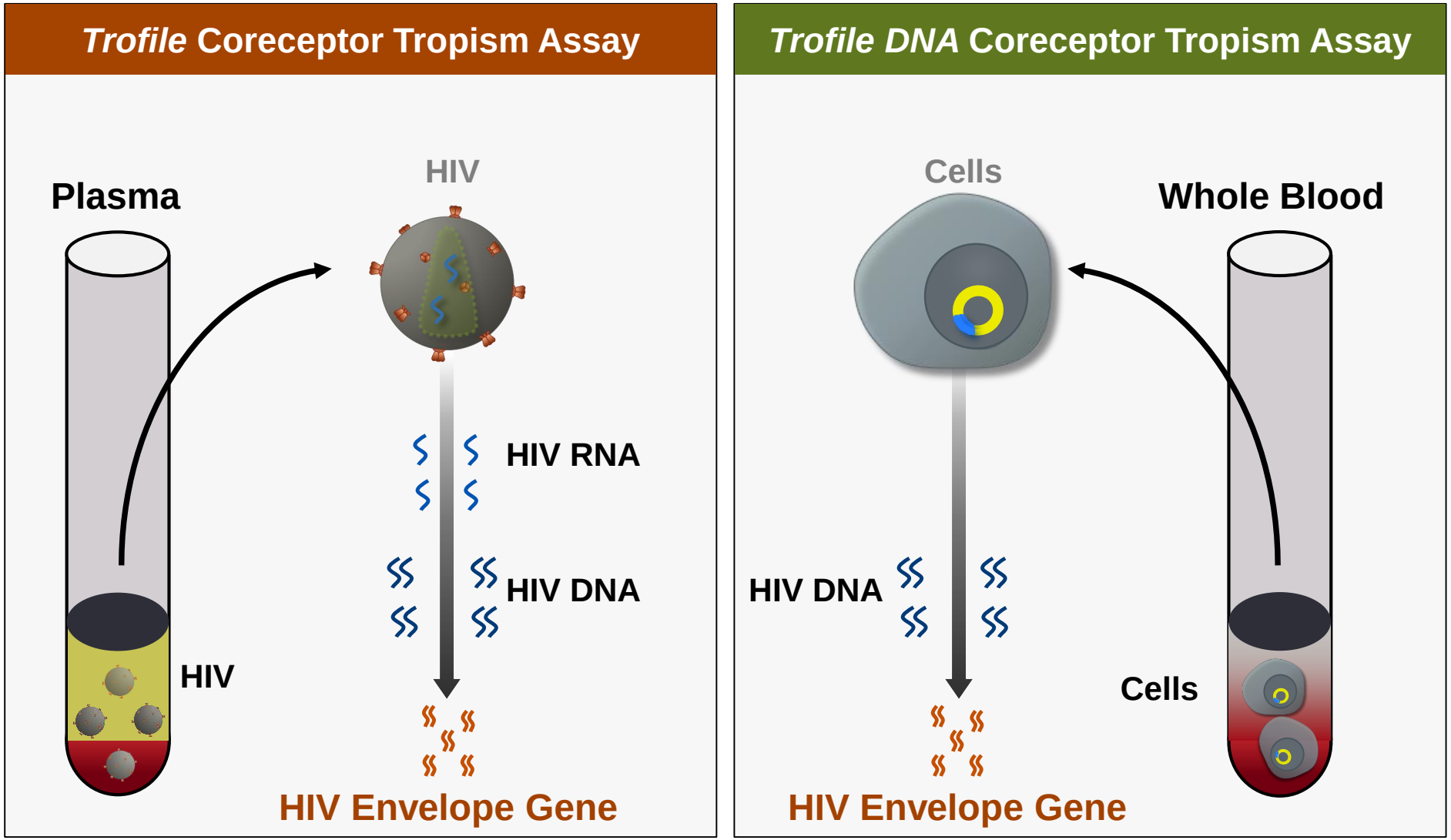


Trofile Coreceptor Tropism Assay



National HIV Curriculum

HIV Coreceptor Tropism Assays (*Trofile*)
Standard and DNA Tropism Assays



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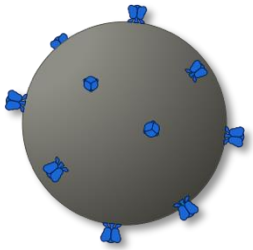
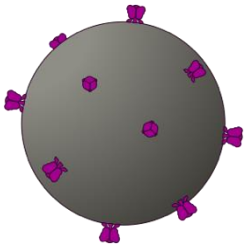
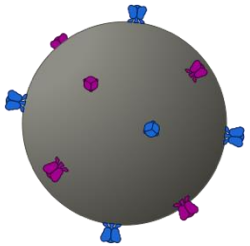
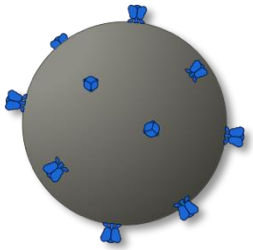
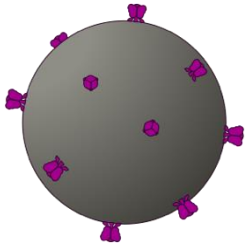
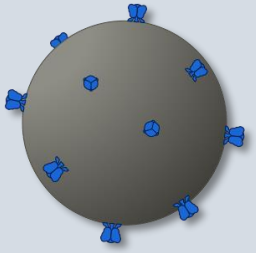
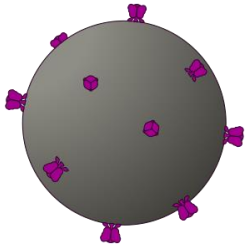
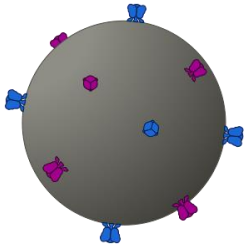
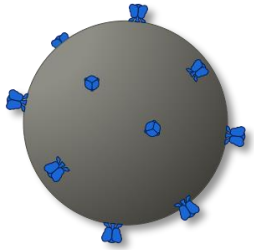
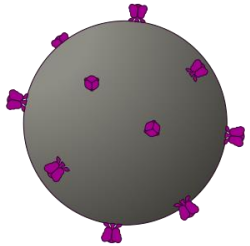
Coreceptor Tropism

R5	X4	Dual Tropic	Mixed Tropic
			 

Pure R5 HIV Result with Coreceptor Tropism Testing

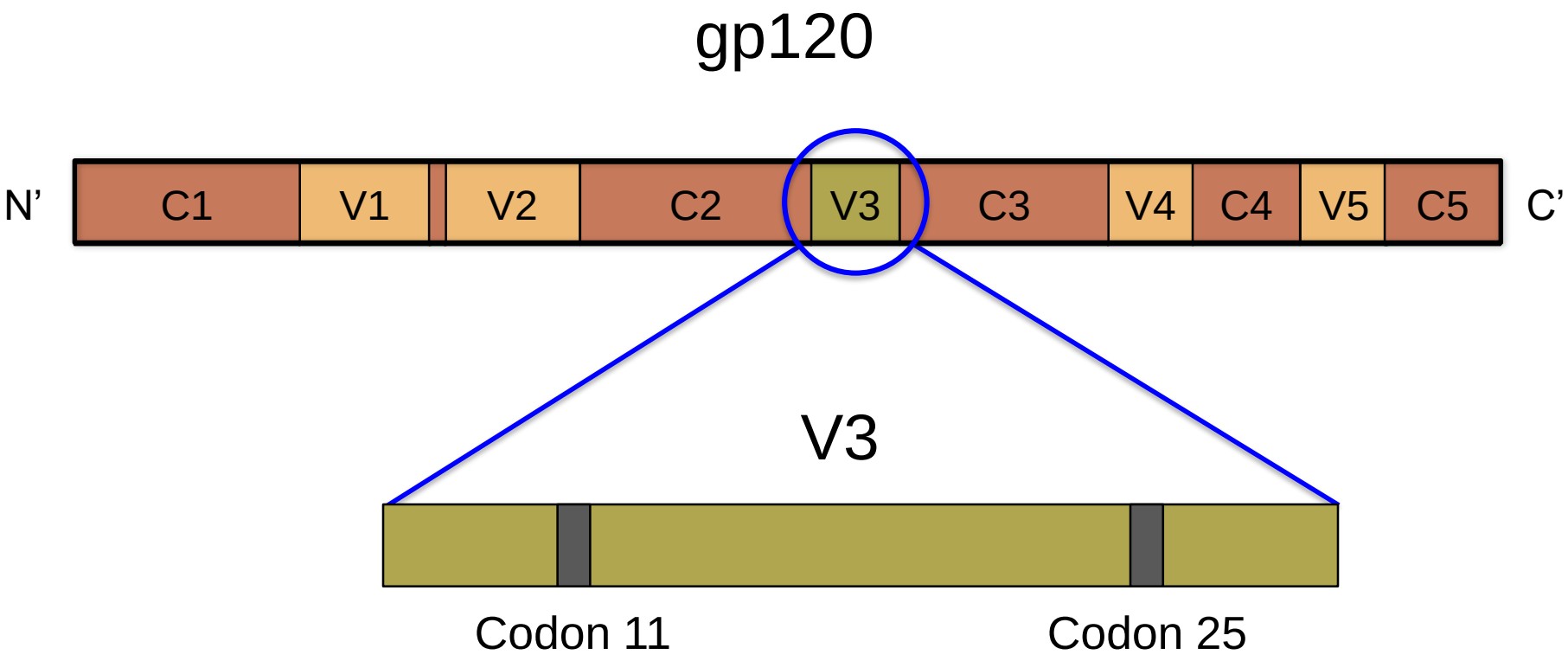
R5	X4	Dual/Mixed Tropic	
		Dual-Tropic HIV	Mixed-Tropic HIV
			
Pure R5 Tropic HIV			

HIV Genotypic Coreceptor Tropism Assay

- Genotypic analysis of gp120 V3 loop sequences
- Commercially available through Quest Diagnostics
- If initial test shows X4 or R5/X4 then no further analysis
- If initial test shows only R5 then reflexes to Ultradeep sequencing
- Detection of 0.5% minority X4 clones with Ultradeep sequencing
- Result available in 7-10 days
- Proviral HIV genotypic tropism assay available (if HIV RNA < 1,000 copies/ml)

Source: Quest Diagnostics: http://education.questdiagnostics.com/faq/FAQ86

HIV Envelope



Source: Tilton JC, Doms RW. Antiviral Research. 2010;85:91-100.

HHS Antiretroviral Therapy Guidelines: October 25, 2018
Recommendation for Co-receptor Tropism Assays

HHS Panel's Recommendation for Co-receptor Tropism Assays	
Recommendation	**Rating**
A co-receptor tropism assay should be performed whenever the use of a CCR5 co-receptor antagonist is being considered	**AI**
Co-receptor tropism testing is also recommended for patients who exhibit virologic failure on a CCR5 antagonist	**BIII**
A phenotypic assay is preferred to determine HIV-1 co-receptor usage	**AI**
A genotypic tropism assay should be considered as an alternative test to predict HIV-1 co-receptor usage	**BII**
A proviral DNA tropism assay can be utilized for patients with undetectable HIV-1 RNA when a CCR5 antagonist is considered in a new regimen (e.g., as part of a regimen switch or simplification)	**BII**

Source: HHS Antiretroviral Guidelines (October 25, 2018).

Maraviroc
Summary of Key Studies

- Trials in Treatment Naïve
  - MERIT: Maraviroc + ZDV-3TC versus Efavirenz + ZDV-3TC
  - A5303: [Maraviroc or Tenofovir DF] + DRV + RTV + FTC
  - A4001078: [Maraviroc or TDF-FTC] + Ritonavir-Boosted Atazanavir
- Trials in Acute HIV
  - OPTIPRIM-ARNS147: 5-Drug versus 3-Drug Regimen for Acute HIV
- Trials in Treatment Experienced
  - MOTIVATE 1 and MOTIVATE 2: Maraviroc [QD or BID] + OBR
  - A4001029: Maraviroc in Treatment-Experienced with non-R5 HIV

Maraviroc
Summary of Key Studies

- Switch Trials
  - Study 121 (Strategy NNRTI): NNRTI Switch to EVG-COBI-TDF-FTC
  - MARCH: Switch to of Maraviroc from RTV-Boosted PI
  - ROCnROL (ARNS 157): Switch to 2-drug Maraviroc + Raltegravir
- Addition of Maraviroc to Increase CD4 Cell Count
  - ACTG 5256: Adding Maraviroc for Suboptimal CD4 Recovery
- PreExposure Prophylaxis
  - HPTN 069/ACTG 5305: Maraviroc +/- [TDF or FTC] for PrEP

INITIAL THERAPY

Maraviroc

Maraviroc versus Efavirenz in Treatment-Naïve

MERIT (A4001026) Trial

Maraviroc versus Efavirenz, both with Zidovudine-Lamivudine
MERIT (A4001026): Study Design

Study Design: MERIT Study

- **Background**: Randomized, double-blind, double-dummy, phase 2b/3 study evaluating the efficacy and safety of maraviroc versus efavirenz as part of ART for treatment-naïve persons with HIV infection
- **Inclusion Criteria (n = 721 treated)**
  - Age ≥16
  - Antiretroviral-naïve patients
  - R5-tropic virus
  - HIV RNA ≥2000 copies/mL
  - No resistance to zidovudine, lamivudine, or efavirenz
- **Treatment Arms**
  - Maraviroc 300 mg BID + ZVD-3TC BID
  - Efavirenz 600 mg QD+ ZVD-3TC BID

MVC 300 mg twice daily + ZVD-3TC twice daily
(n = 360)

EFV once daily + ZVD-3TC twice daily
(n =361)

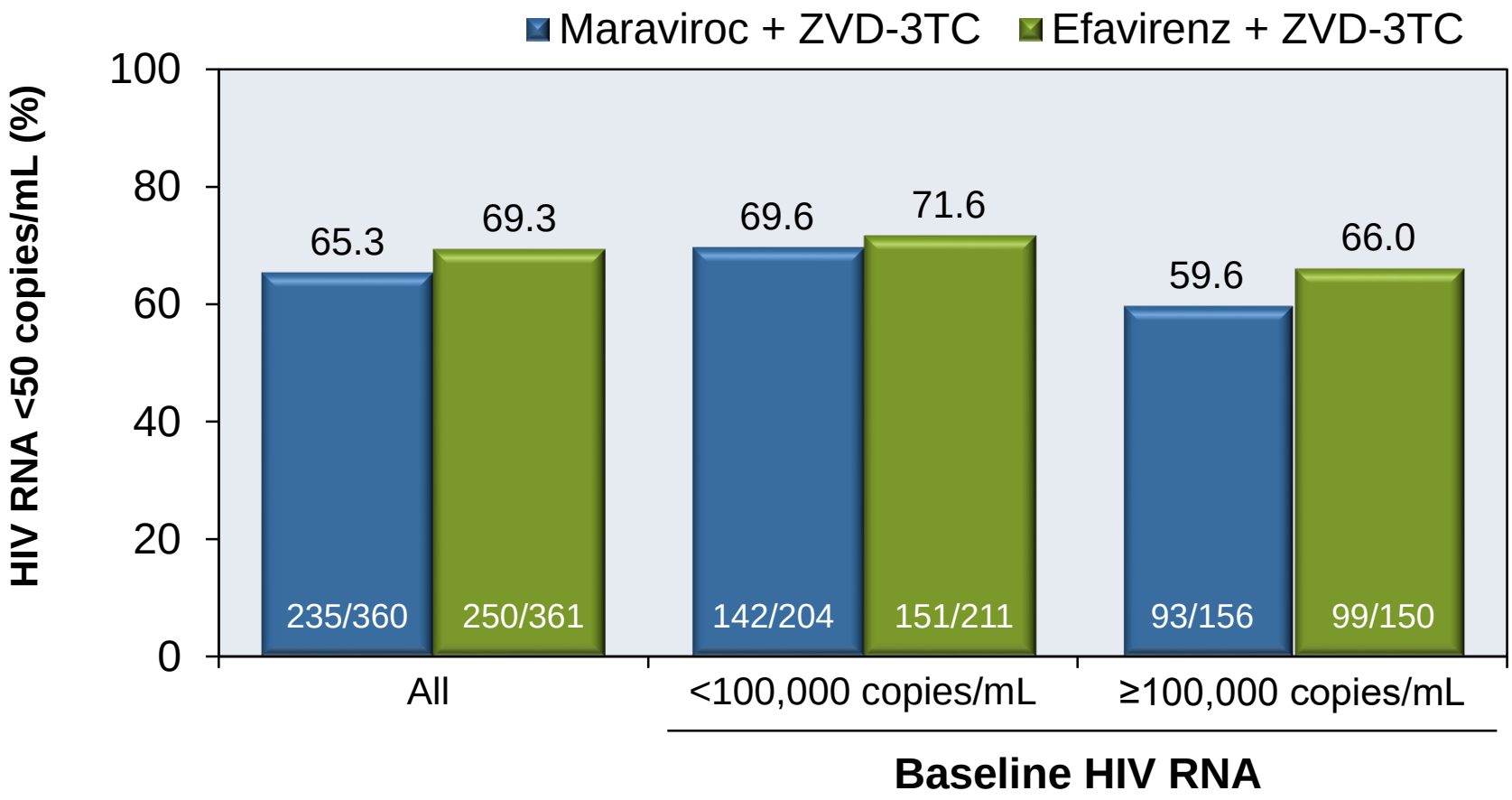
MVC 300 mg once daily + ZVD-3TC twice daily arm (n = 174)
DISCONTINUED at interim analysis

MERIT = Maraviroc versus Efavirenz in Treatment-Naive

Source: Cooper DA, et al. J Infect Dis. 2010;201:803-13.

Maraviroc versus Efavirenz, both with Zidovudine-Lamivudine
MERIT (A4001026): Result

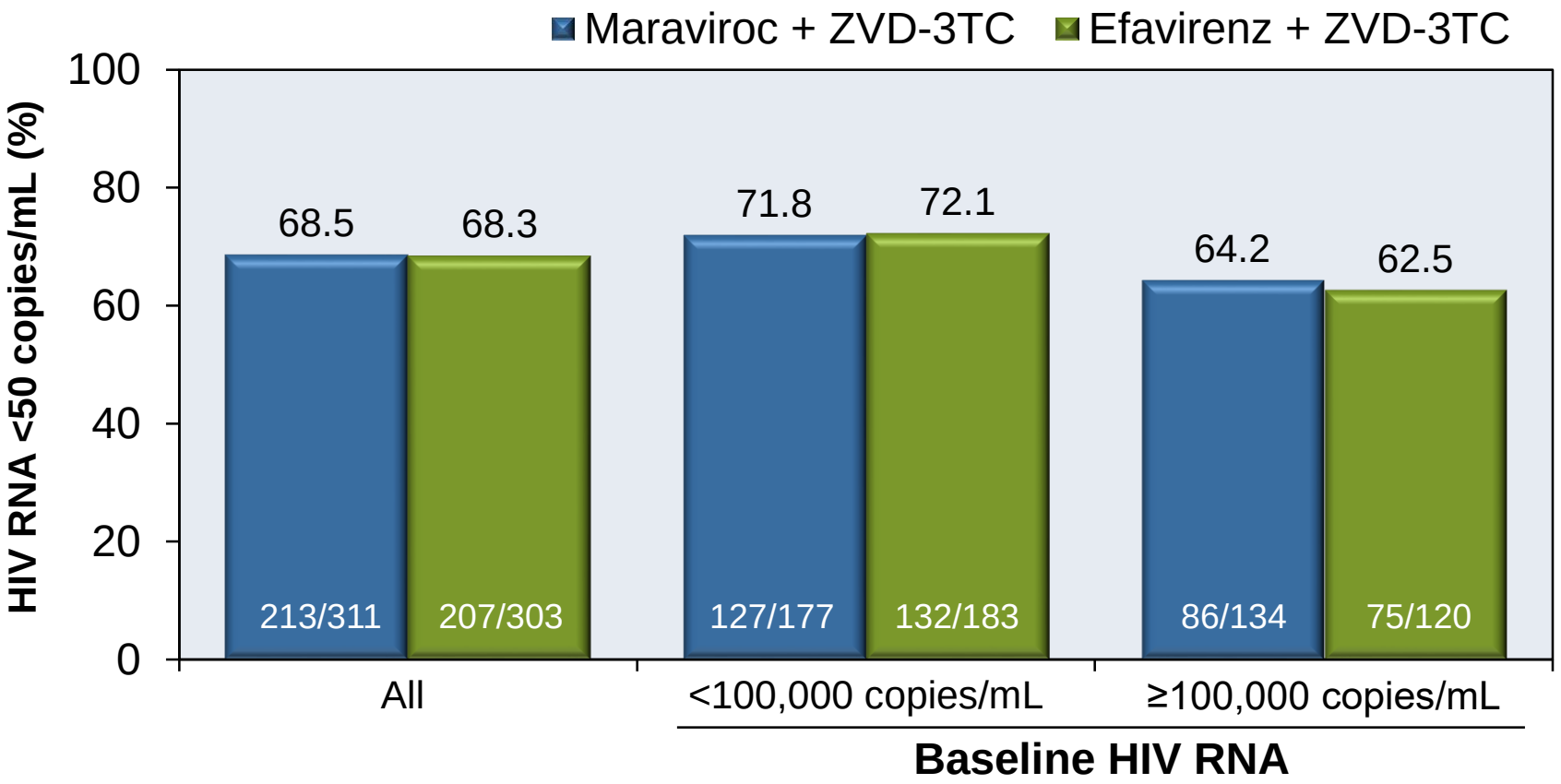
Week 48: Virologic Response (Primary Analysis)



Source: Cooper DA, et al. J Infect Dis. 2010;201:803-13.

Maraviroc or Efavirenz, both with Zidovudine-Lamivudine
MERIT (A4001026): Result

Week 48: Virologic Response (Post-hoc Reanalysis*)



*Excludes patients with non-R5 virus at screening by the enhanced Trofile assay

Source: Cooper DA, et al. J Infect Dis. 2010;201:803-13.

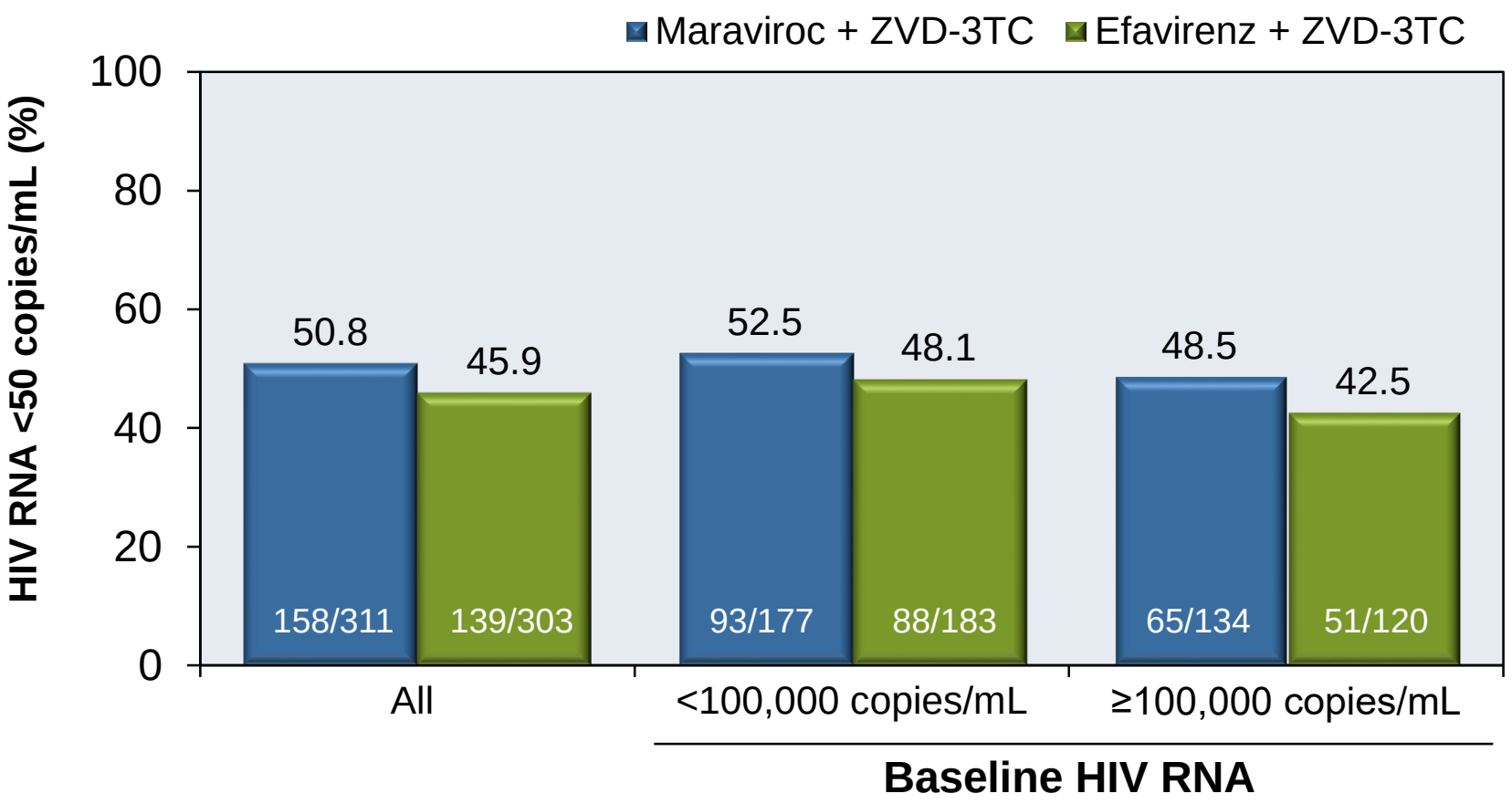
Maraviroc versus Efavirenz, both with Zidovudine-Lamivudine
MERIT (A4001026): Conclusions

Conclusions: “Twice-daily maraviroc was not noninferior to efavirenz at <50 copies/mL in the primary analysis. However, 15% of patients would have been ineligible for inclusion by a more sensitive screening assay. Their retrospective exclusion resulted in similar response rates in both arms.”

Source: Cooper DA, et al. J Infect Dis. 2010;201:803-13.

Maraviroc versus Efavirenz, plus Zidovudine-Lamivudine MERIT (A4001026): Results

Week 240 (Year 5): Virologic Response



*Excludes patients with non-R5 virus at screening by the enhanced Trofile assay

Source: Cooper DA, et al. AIDS. 2014;28:717-25.

Maraviroc versus Efavirenz, plus Zidovudine-Lamivudine
MERIT (A4001026) Year 5 Data: Conclusions

Conclusions: “Maraviroc maintained similar long-term antiviral efficacy to efavirenz over 5 years in treatment-naive patients with CCR5-tropic HIV-1. Maraviroc was generally well tolerated with no unexpected safety findings or evidence of long-term safety concerns.”

Source: Cooper DA, et al. AIDS. 2014;28(5):717-25.

Effects of Maraviroc versus Tenofovir DF on Bone Loss
A5303 Trial

Bone Effects of Maraviroc vs. Tenofovir DF, with DRV + RTV + FTC

A5303: Study Design

Study Design: A5303 Study

- **Background**: Phase 2b, prospective, double-blind, placebo-controlled study evaluating the effects of maraviroc versus tenofovir DF on bone loss in treatment-naïve persons with HIV
- **Inclusion Criteria (n = 262)**
  - Age ≥18 years
  - Antiretroviral-naïve patients
  - R-5 tropic virus
  - HIV RNA >1000 copies/mL
- **Treatment Arms***
  - MVC + DRV + RTV + FTC
  - TDF + DRV + RTV + FTC

MVC + DRV + RTV + FTC
(n = 130)

TDF + DRV + RTV + FTC
(n = 129)

*Dosing: Maraviroc 150 mg QD + Darunavir 800 mg QD + Ritonavir 100 mg QD + Emtricitabine 200 mg QD

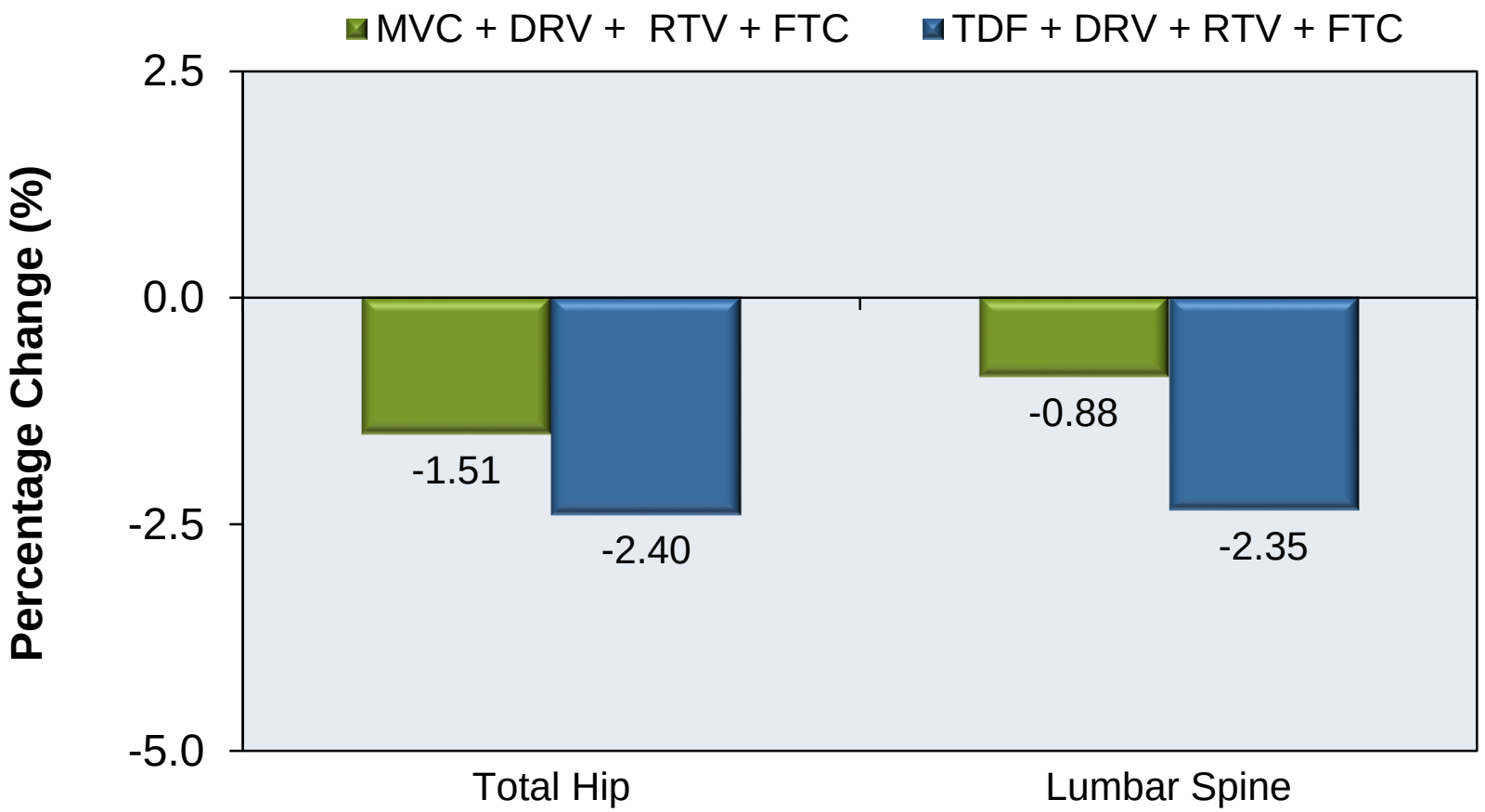
*Dosing: Tenofovir 300 mg QD + Emtricitabine 200 mg QD + Darunavir 800 mg QD + Ritonavir 100 mg QD

Source: Taiwo B, et al. Clin Infect Dis. 2015;61:1179-88.

Bone Effects of Maraviroc vs. Tenofovir DF, with DRV + RTV + FTC

A5303: Results

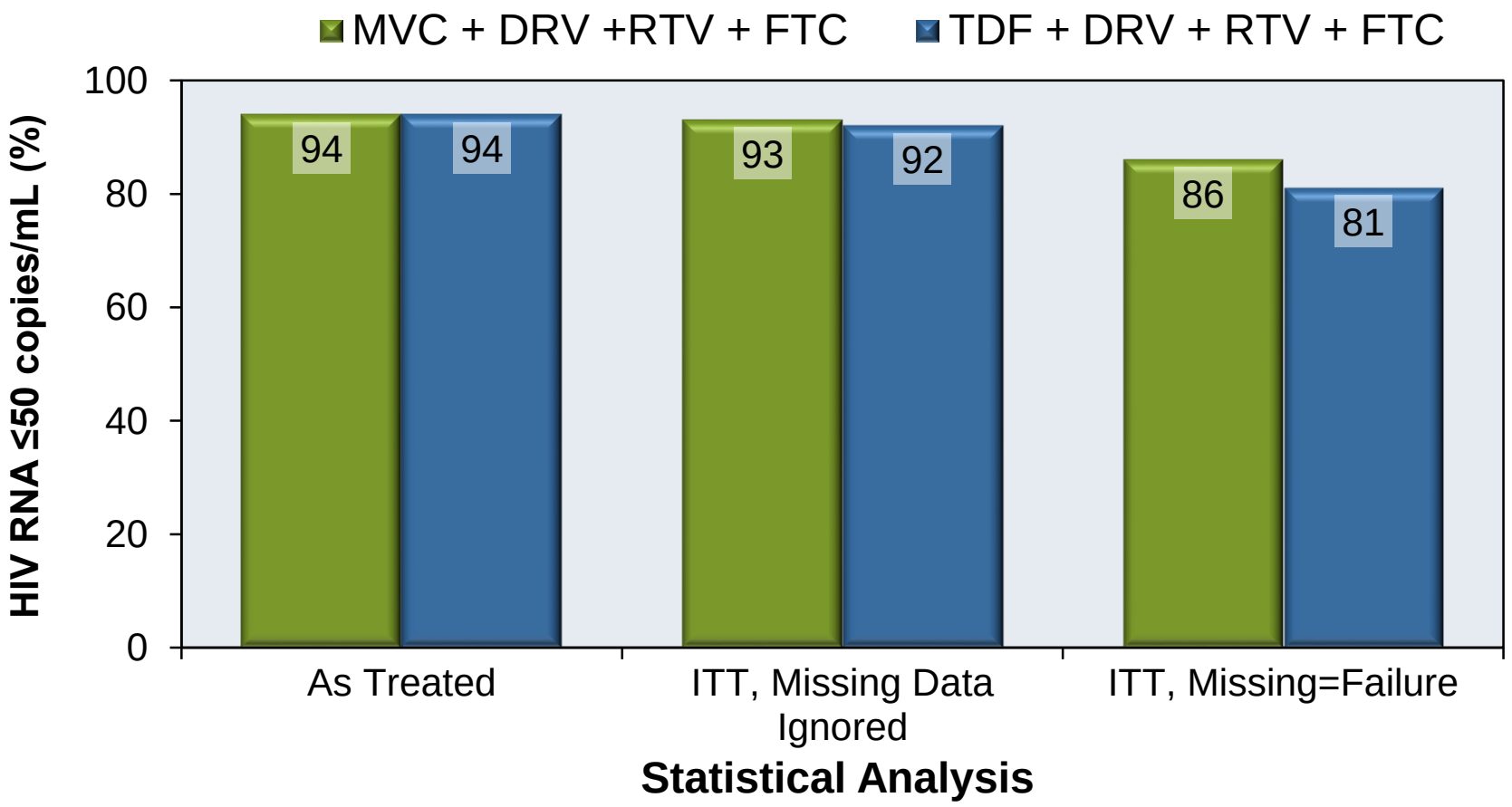
Week 48: Changes in Bone Mineral Density from Baseline



Source: Taiwo B, et al. Clin Infect Dis. 2015;61:1179-88.

Bone Effects of Maraviroc vs. Tenofovir DF, with DRV + RTV + FTC
A5303: Results

Week 48: Virologic Response



Source: Taiwo B, et al. Clin Infect Dis. 2015;61:1179-88.

Bone Effects of Maraviroc vs. Tenofovir DF, with DRV + RTV + FTC
A5303: Conclusions

Conclusions: “Maraviroc was associated with less bone loss at the hip and lumbar spine compared with tenofovir DF. Maraviroc may be an option to attenuate ART-associated bone loss.”

Source: Taiwo B, et al. Clin Infect Dis. 2015;61:1179-88.

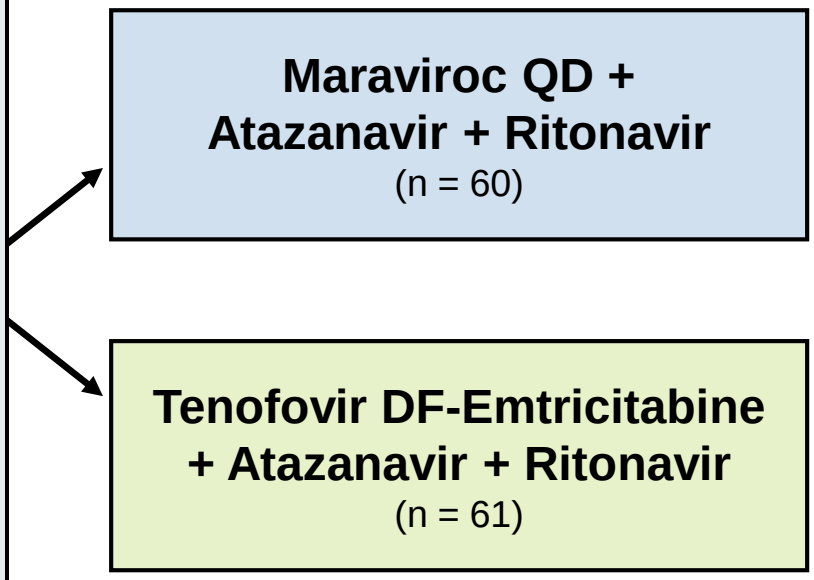
Once-Daily Maraviroc in Treatment-Naïve

A4001078 Trial

Once-Daily Maraviroc plus Ritonavir-Boosted Atazanavir
A4001078: Study Design

Study Design: A4001078 Study

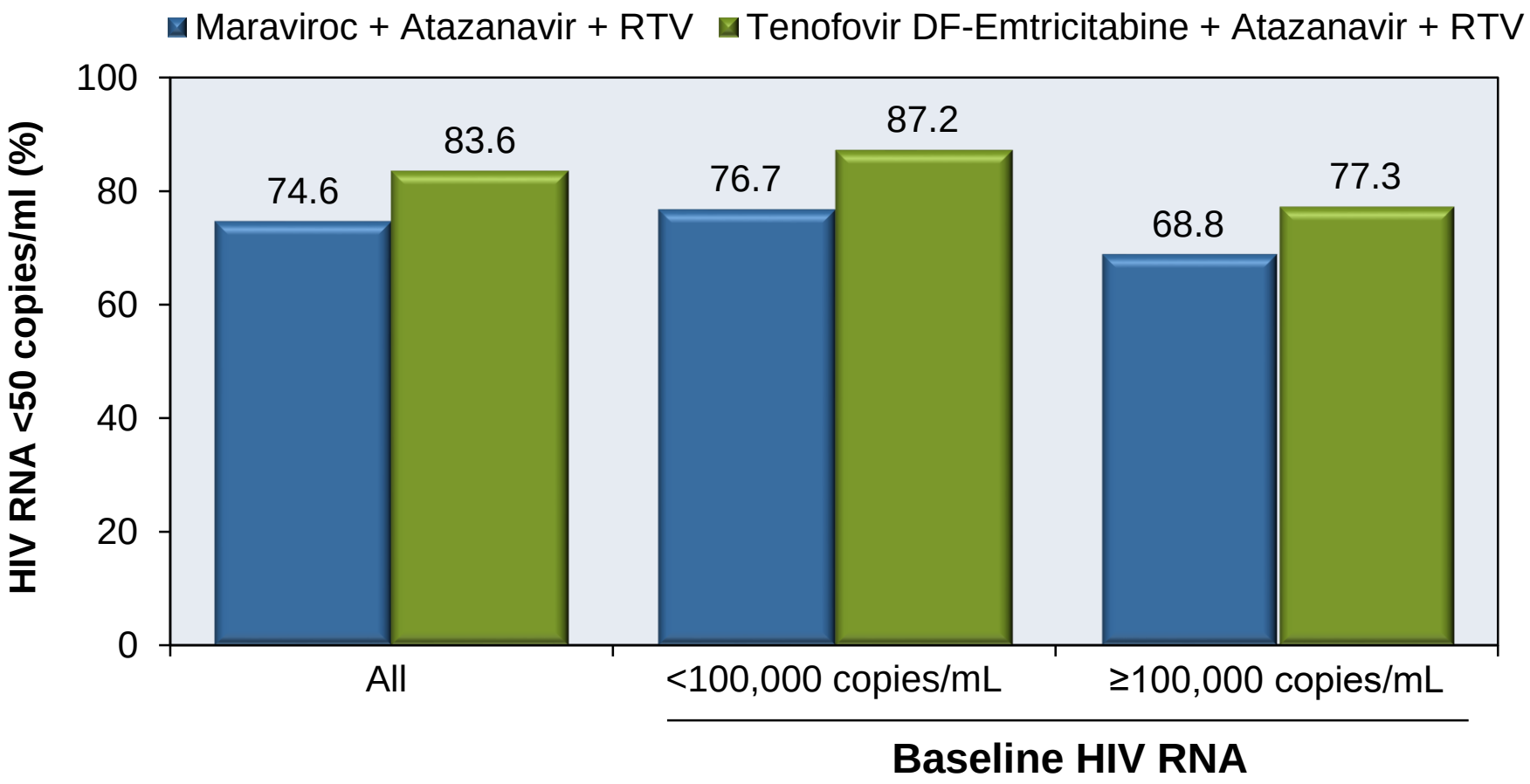
- **Background**: Phase 2b, randomized, open label pilot study evaluating a once-daily, dual-therapy regimen of maraviroc and boosted atazanavir in comparison to standard triple therapy in HIV-infected treatment-naïve patients
- **Inclusion Criteria (n = 121)**
  - Age ≥16 years
  - Antiretroviral-naïve patients
  - R-5 tropic virus
  - HIV RNA ≥1000 copies/mL
  - CD4 ≥100 cells/mm^3
- **Treatment Arms** (all medications once daily)
  - Maraviroc 150 mg + Atazanavir 300 mg + Ritonavir 100 mg
  - Tenofovir DF-Emtricitabine + Atazanavir 300 mg + Ritonavir 100 mg



Source: Mills A, et al. J Acquir Immune Defic Syndr. 2013;62:164-70.

Once-Daily Maraviroc plus Ritonavir-Boosted Atazanavir A4001078: Results

Week 48: Virologic Response (Missing or Discontinued = Failure)



Source: Mills A, et al. J Acquir Immune Defic Syndr. 2013;62:164-70.

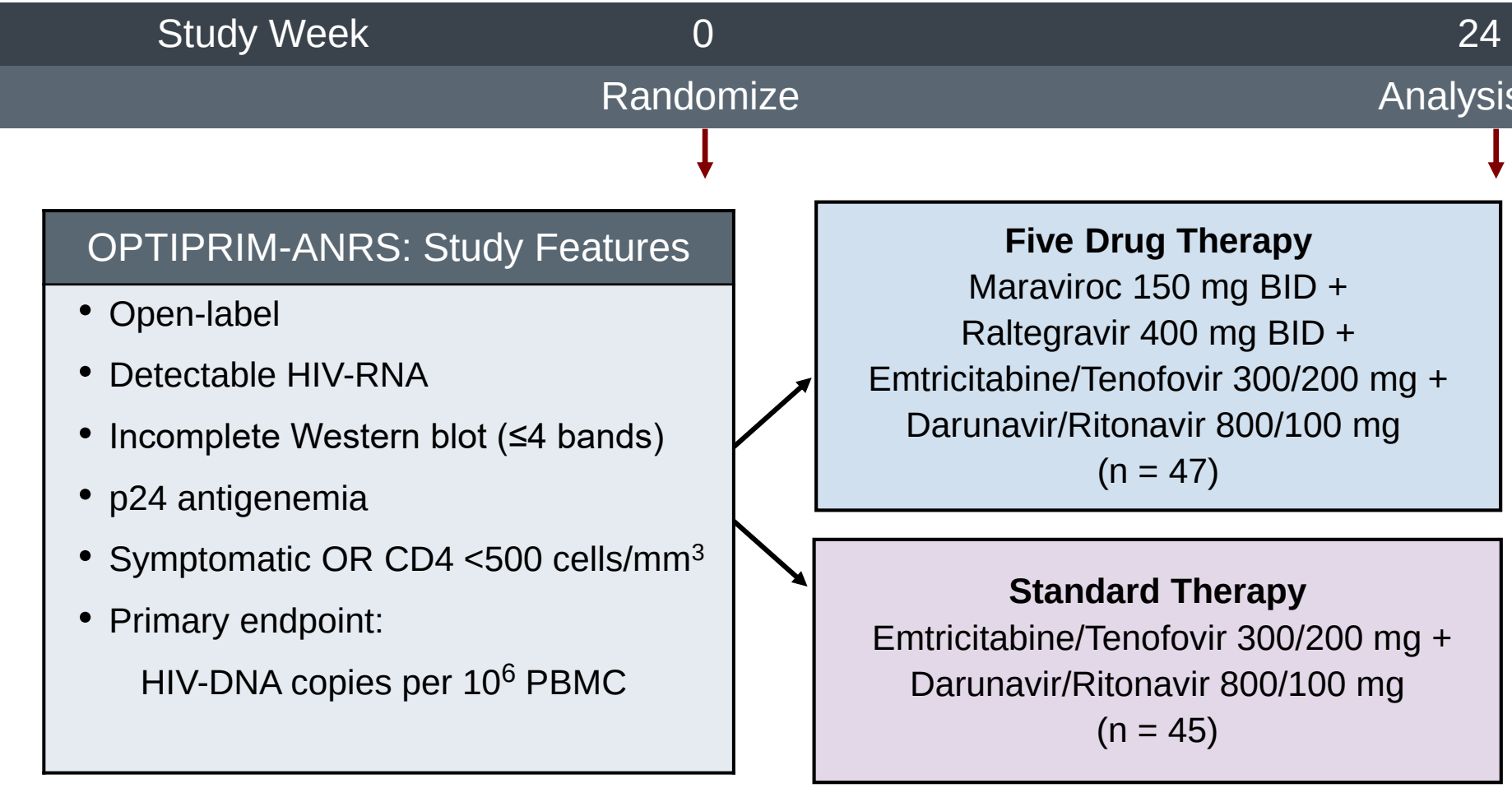
Once-Daily Maraviroc plus Ritonavir-Boosted Atazanavir A4001078: Conclusions

Conclusions: “The virological activity and immunological benefit of once-daily MVC + ATV/r were confirmed. Indirect hyperbilirubinemia and associated signs were the most commonly reported adverse effects in both study treatment groups and were not associated with significant transaminase increases. No drug resistance occurred.”

Source: Mills A, et al. J Acquir Immune Defic Syndr. 2013;62:164-70.

Intensive Five-Drug Regimen for Acute HIV Infection
OPTIPRIM-ANRS147

Five Drug Therapy versus Standard Care for Acute HIV
OPTIPRIM-ANRS 147 Trial: Study Design

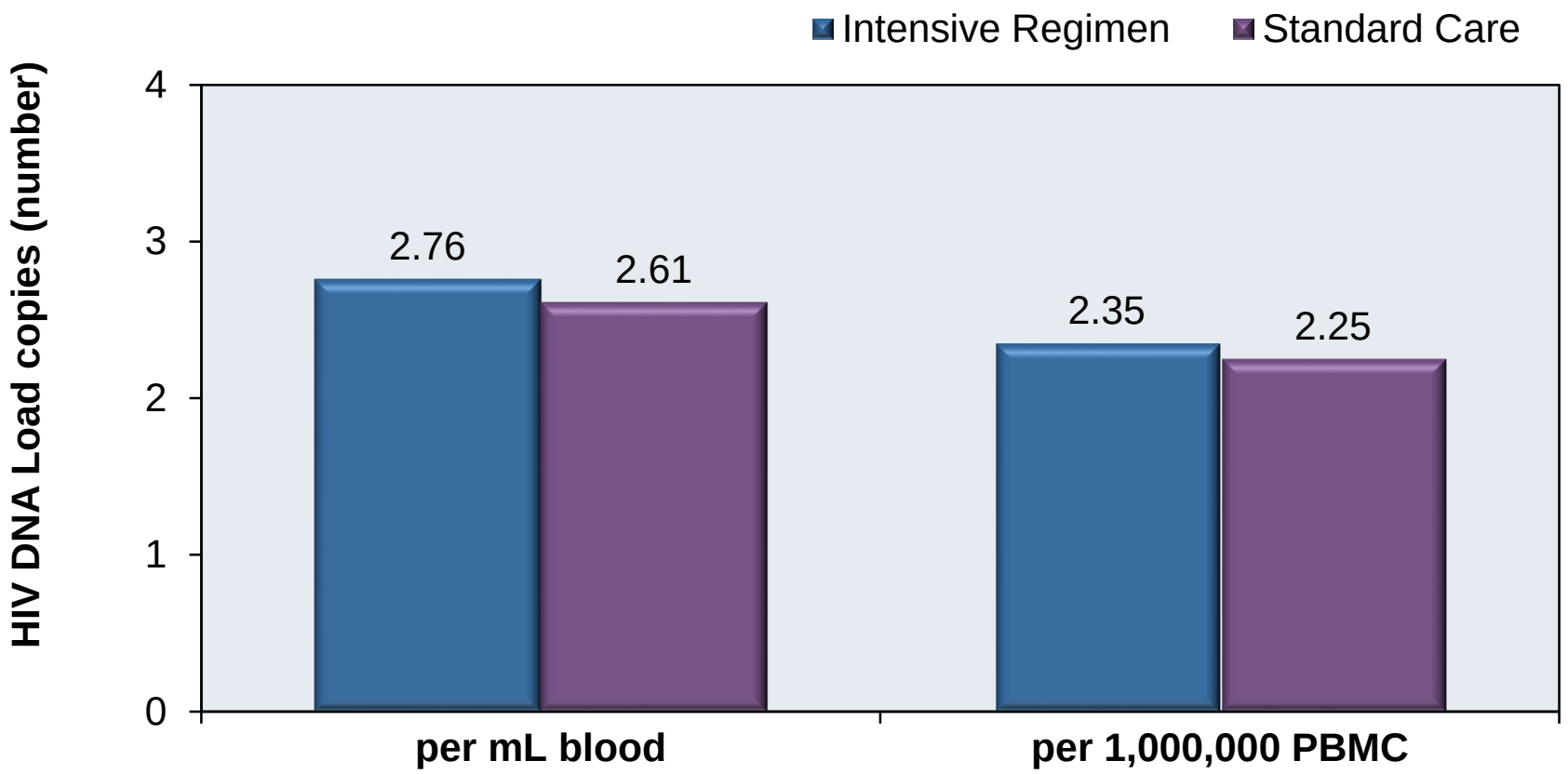


Source: Chéret A, et al. Lancet Infect Dis. 2015;15:387-96.

National HIV Curriculum

Five Drug Therapy versus Standard Care for Acute HIV
OPTIPRIM-ANRS 147 Trial: Results

HIV DNA Load at Month 24



Source: Chéret A, et al. Lancet Infect Dis. 2015;15:387-96.

Five Drug Therapy versus Standard Care for Acute HIV OPTIPRIM-ANRS 147 Trial: Conclusion

Interpretation: “After 24 months, cART intensified with raltegravir and maraviroc did not have a greater effect on HIV blood reservoirs than did standard cART. These results should help to design future trials of treatments aiming to decrease the HIV reservoir in patients with primary HIV-1 infection.”

Source: Chéret A, et al. Lancet Infect Dis. 2015;15:387-96.

TREATMENT EXPERIENCED

Maraviroc

Maraviroc in Patients with Multiclass Drug Resistance

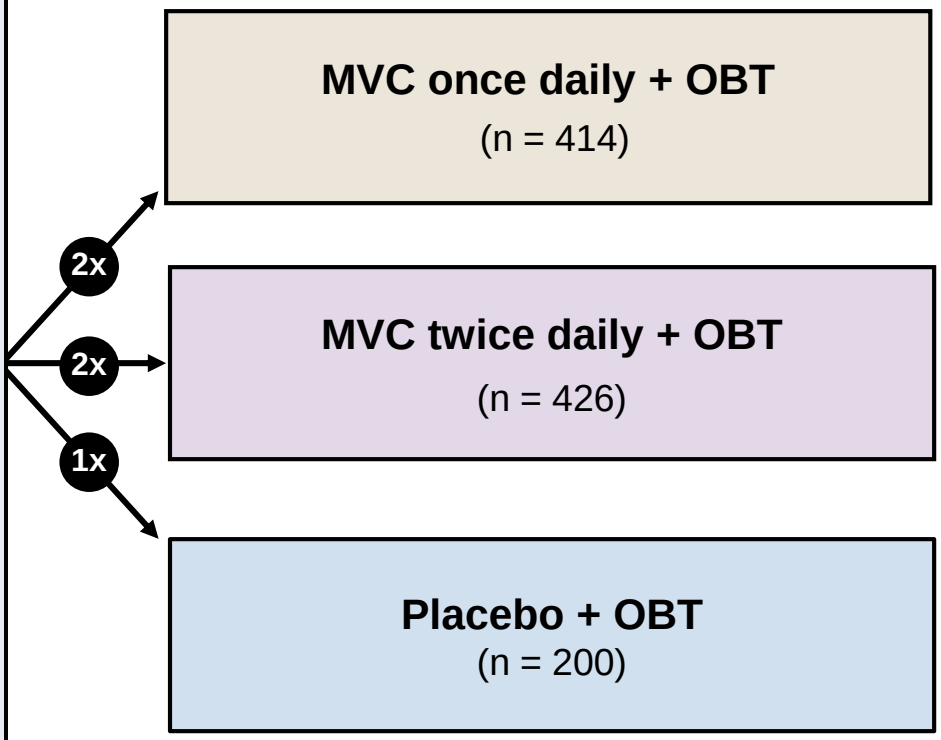
MOTIVATE 1 and 2 Trials

Maraviroc in Patients with Multiclass Drug Resistance
MOTIVATE 1 and 2: Study Design

MOTIVATE = Maraviroc versus Optimized Therapy in Viremic Antiretroviral Treatment-Experienced Patients

Study Design: MOTIVATE 1 and 2

- **Background**: Parallel, randomized, double-blind, placebo-controlled, phase 3 trials to evaluate safety and efficacy of maraviroc in treatment-experienced patients
- **Inclusion Criteria (n = 1049)**
  - Age ≥ 16
  - Resistance to ≥ 3 ARV classes
  - R-5 tropic virus
  - On stable ARV regimen or no regimen for ≥ 4 weeks with HIV RNA ≥ 5000 copies/mL
- **Treatment Arms**
  - Maraviroc* once daily + OBT**
  - Maraviroc* twice daily + OBT**
  - Placebo + OBT**

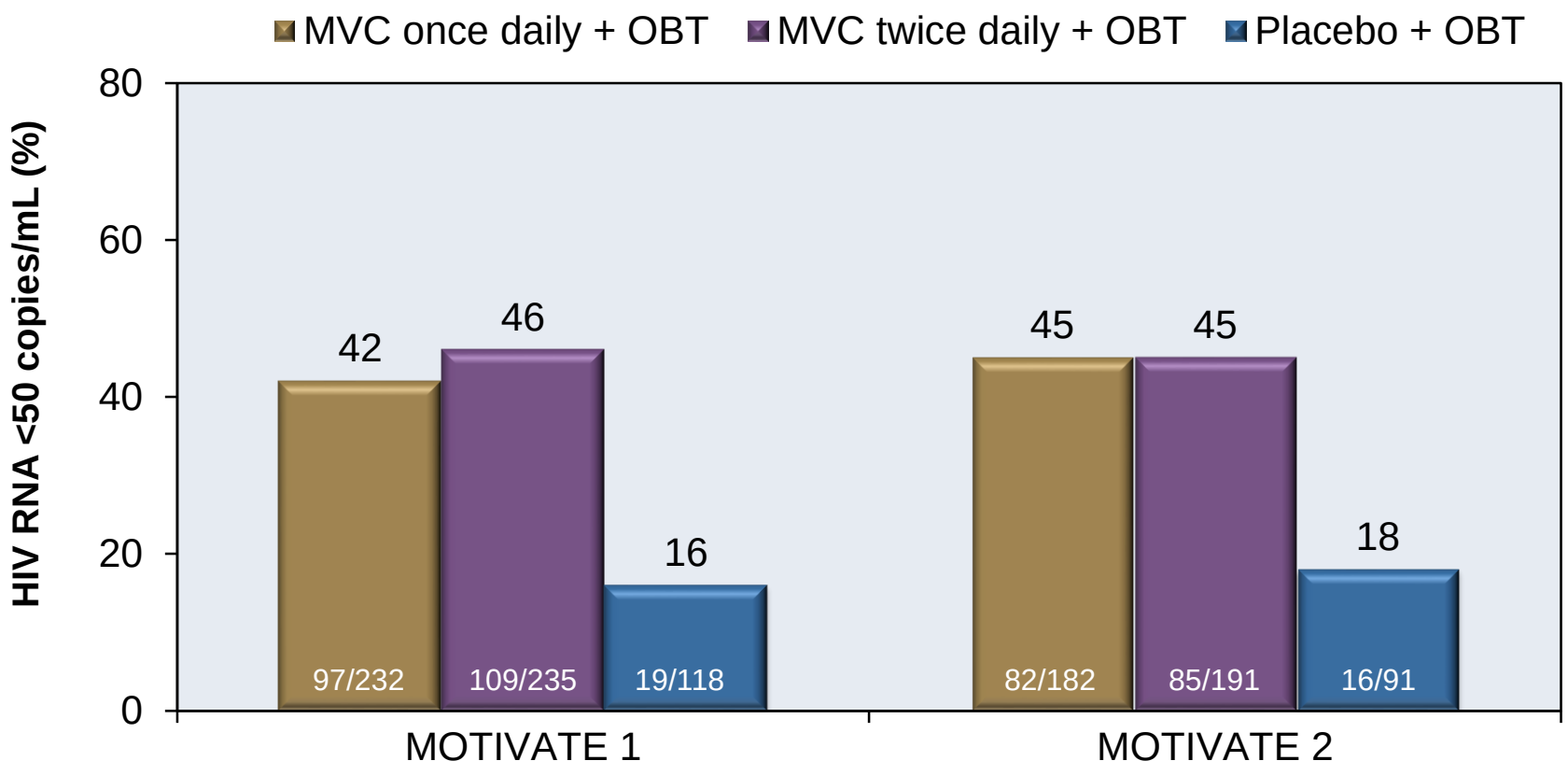


*MVC dose 300mg daily or BID with PI-containing regimens, 150mg daily or BID with all other regimens
**OBT= Optimized Background Therapy (investigator-selected, 3-6 agents).

Source: Gulick RM, et al. N Engl J Med. 2008;359:1429-41.

Maraviroc in Patients with Multiclass Drug Resistance
MOTIVATE 1 and 2: Results

Week 48: Virologic Response (ITT, missing=nonresponse)



Source: Gulick RM, et al. N Engl J Med. 2008;359:1429-41.

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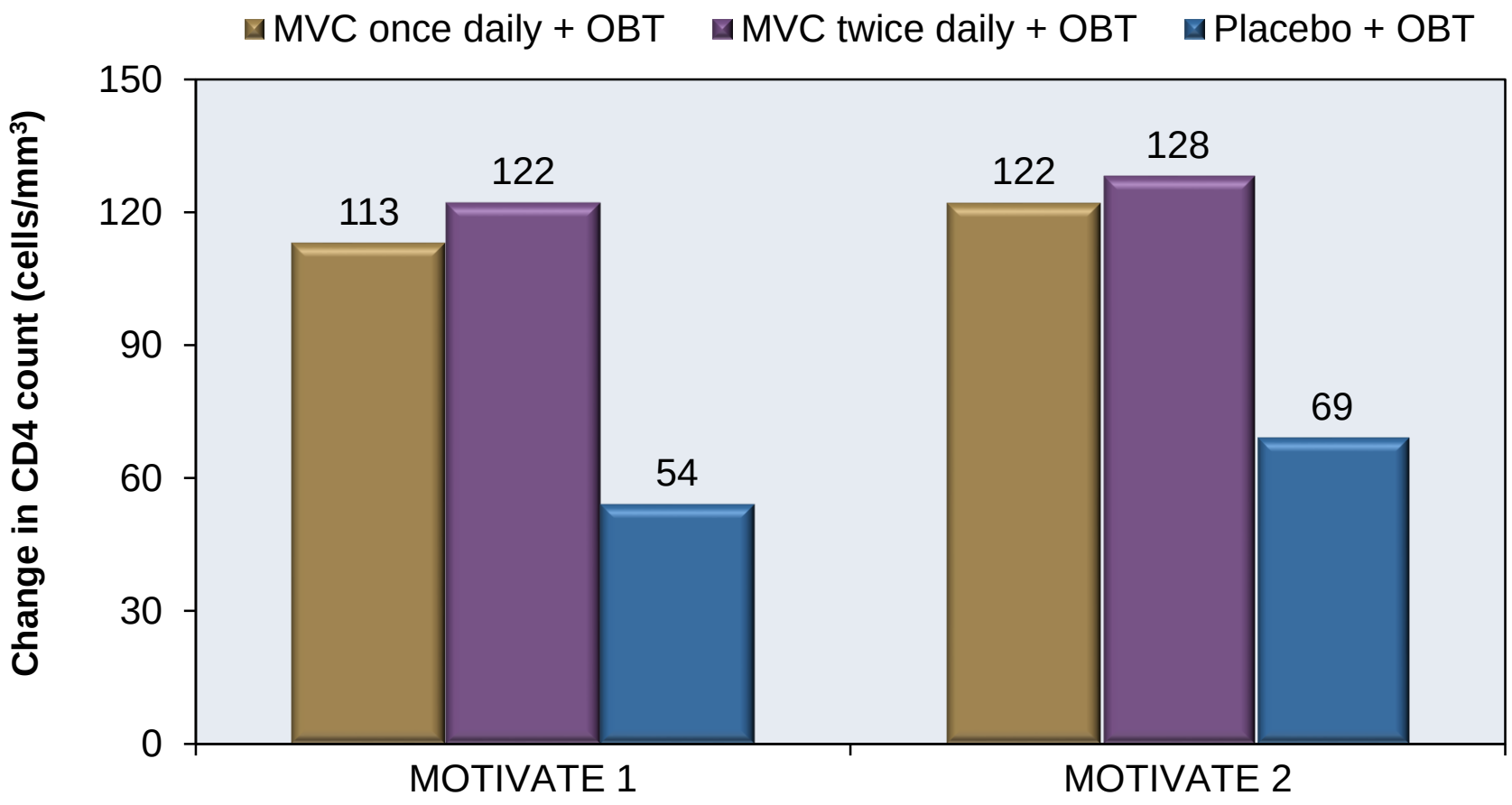
Maraviroc in Patients with Multiclass Drug Resistance
MOTIVATE 1 and 2: Results

Week 48: Change in CD4 Cell Count from Baseline



Source: Gulick RM, et al. N Engl J Med. 2008;359:1429-41.

Maraviroc in Patients with Multiclass Drug Resistance
MOTIVATE 1 and 2: Result

Grade 2-4 Adverse Events (all causes) Occurring in ≥ 5% of Patients
(MOTIVATE 1 and MOTIVATE 2 Study Populations Combined)

	Maraviroc once daily + OBT (n = 414)	**Maraviroc twice daily + OBT** (n = 426)	**Placebo** (n = 219)
Diarrhea	43 (10%)	32 (8%)	20 (10%)
Fatigue	13 (3%)	21 (4%)	13 (6%)
Fever	9 (2%)	24 (6%)	9 (4%)
Headache	22 (5%)	9 (2%)	12 (6%)
Nausea	25 (6%)	25 (6%)	15 (7%)
Upper respiratory infection	16 (4%)	20 (5%)	3 (1%)
Death	6 (1%)	9 (2%)	2 (1%)

Source: Gulick RM, et al. N Engl J Med. 2008;359:1429-41.

Maraviroc in Patients with Multiclass Drug Resistance
MOTIVATE 1 and 2: Conclusions

Conclusions: “Maraviroc, as compared with placebo, resulted in significantly greater suppression of HIV-1 and greater increases in CD4 cell counts at 48 weeks in previously treated patients with R5 HIV-1 who were receiving OBT.”

Source: Gulick RM, et al. N Engl J Med. 2008;359:1429-41.

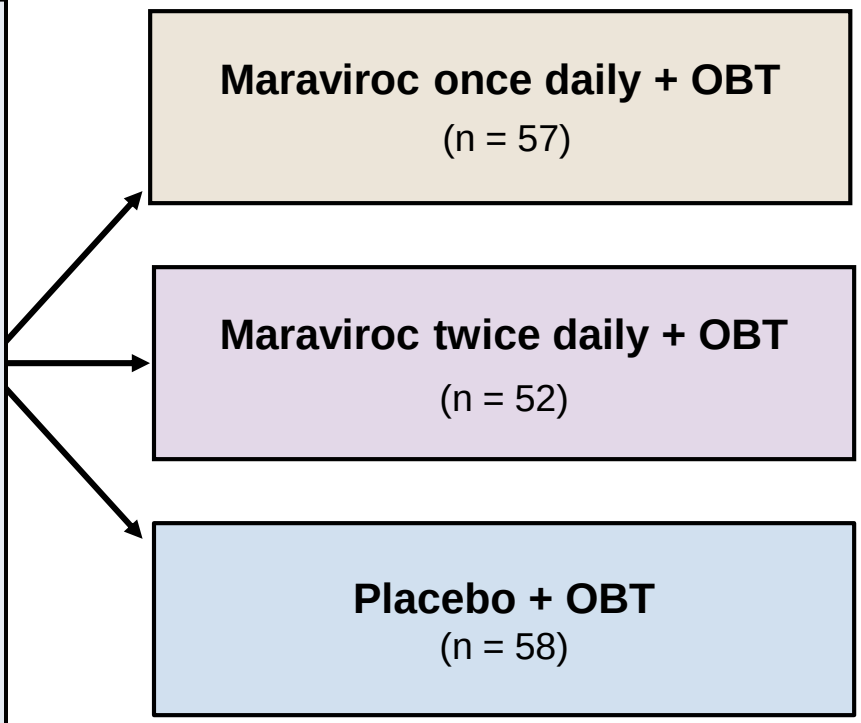
Maraviroc in Treatment-Experienced Patients with non-R5 HIV

A4001029 Trial

Maraviroc in Treatment-Experienced Patients with non-R5 HIV
A4001029: Study Design

Study Design: A4001029

- **Background**: Randomized, double-blind, placebo-controlled, phase 2b trials to evaluate safety and efficacy of maraviroc in treatment-experienced patients infected with non-R5 tropic HIV
- **Inclusion Criteria (n = 190)**
  - Resistance to ≥2 ARV classes, or ≥3 months of treatment ≥3 ARV classes
  - X4, dual, or mixed-tropic HIV
- **Treatment Arms**
  - Maraviroc 300 mg once daily + OBT*
  - Maraviroc 300 mg twice daily + OBT*
  - Placebo + OBT*

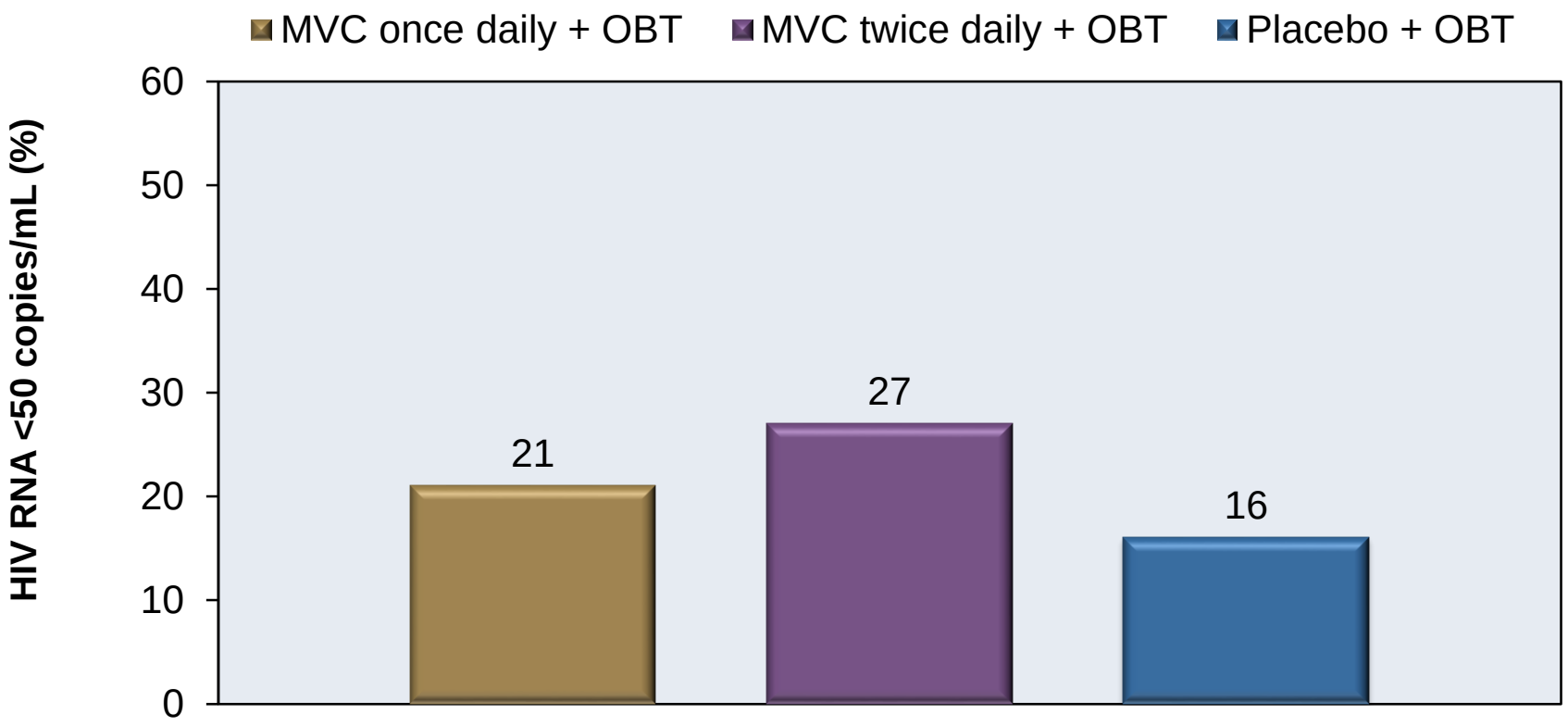


*OBT = Optimized Background Therapy (investigator selected, 3-6 agents). MVC dose reduced to 150 mg (daily or BID) in patients taking protease inhibitors (except tipranavir) or delavirdine.

Source: Saag M, et al. J Infect Dis. 2009;199:1638-47.

Maraviroc in Treatment-Experienced Patients with non-R5 HIV
A4001029: Results

Week 24: Virologic Response*

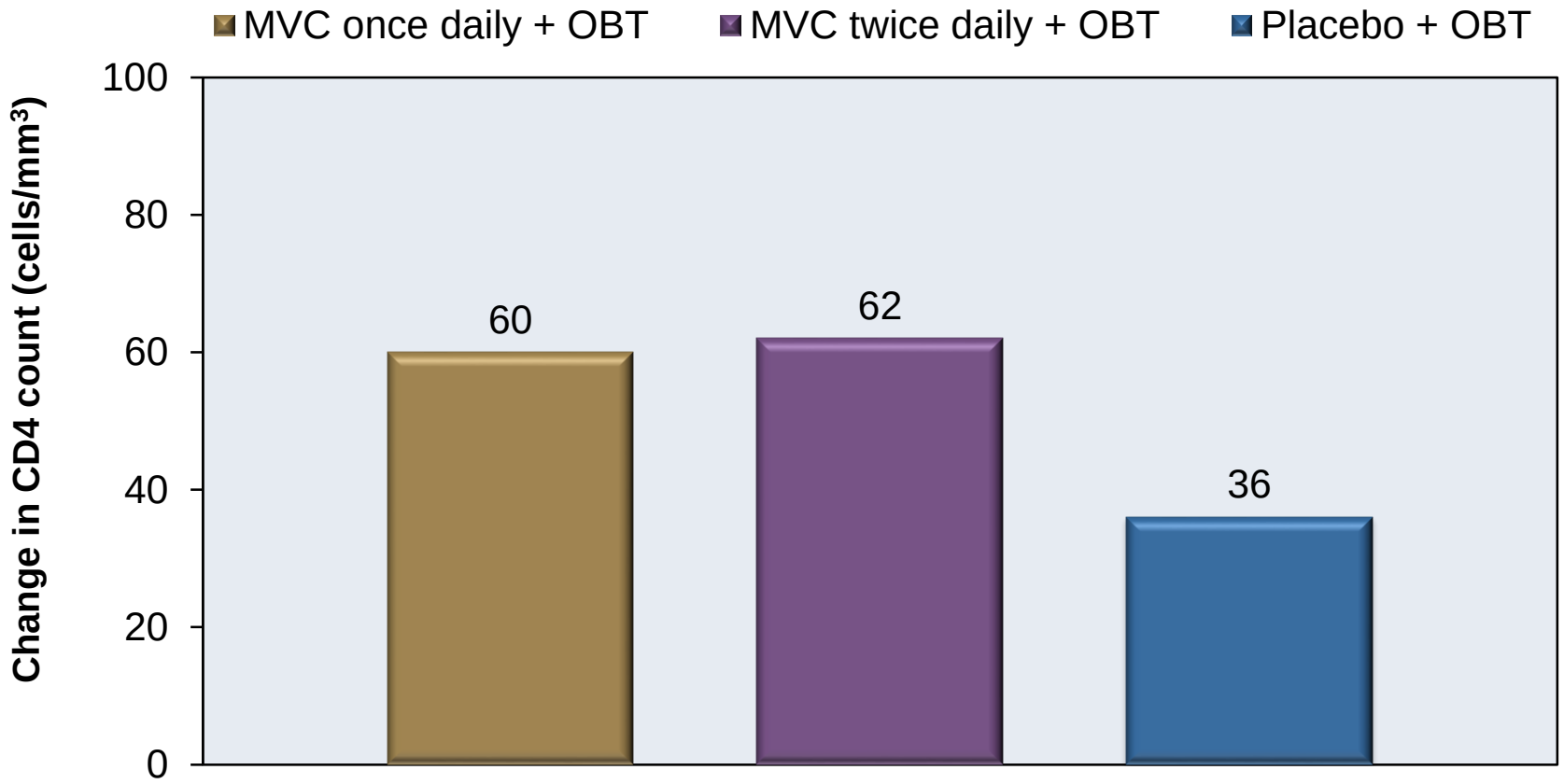


*Values for patients with missing data or who discontinued treatment imputed as 0

Source: Saag M, et al. J Infect Dis. 2009;199:1638-47.

Maraviroc in Treatment-Experienced Patients with non-R5 HIV
A4001029: Results

Week 24: Change in CD4 Cell Count from Baseline*



*Using last observation carried forward method

Source: Saag M, et al. J Infect Dis. 2009;199:1638-47.

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Maraviroc in Treatment-Experienced Patients with non-R5 HIV
A4001029: Conclusions

Conclusions: “In this exploratory study involving extensively treatment-experienced patients with advanced, non-R5 HIV-1 infection, neither superiority nor noninferiority was statistically demonstrated for either maraviroc dosage compared with placebo at 24 weeks of treatment.”

Source: Saag M, et al. J Infect Dis. 2009;199:1638-47.

Adding Maraviroc to Suppressive ART for Suboptimal CD4 Recovery

ACTG 5256

ACTG 5256: Study Design

Study Design: ACTG 5256

- **Background**: Single-arm, pilot trial of adding maraviroc to suppressive ART in setting of suboptimal CD4 recovery to evaluate whether maraviroc intensification is associated with an increase of at least 20 cells/mm^3 in the CD4 count
- **Inclusion Criteria (n = 34)**
  - HIV-1 infected adults
  - Receiving stable ART with HIV RNA below limit of detection for at least 48 weeks
  - Stable but suboptimal CD4 recovery over previous year (<250 cells/mm^3 and slope of annual change between -20 and 20 cells/mm^3)
  - No prior exposure to a CCR5 antagonist
- **Single Treatment Arm**
  - Maraviroc added to ART for 24 weeks, then stopped and patient followed another 24 weeks

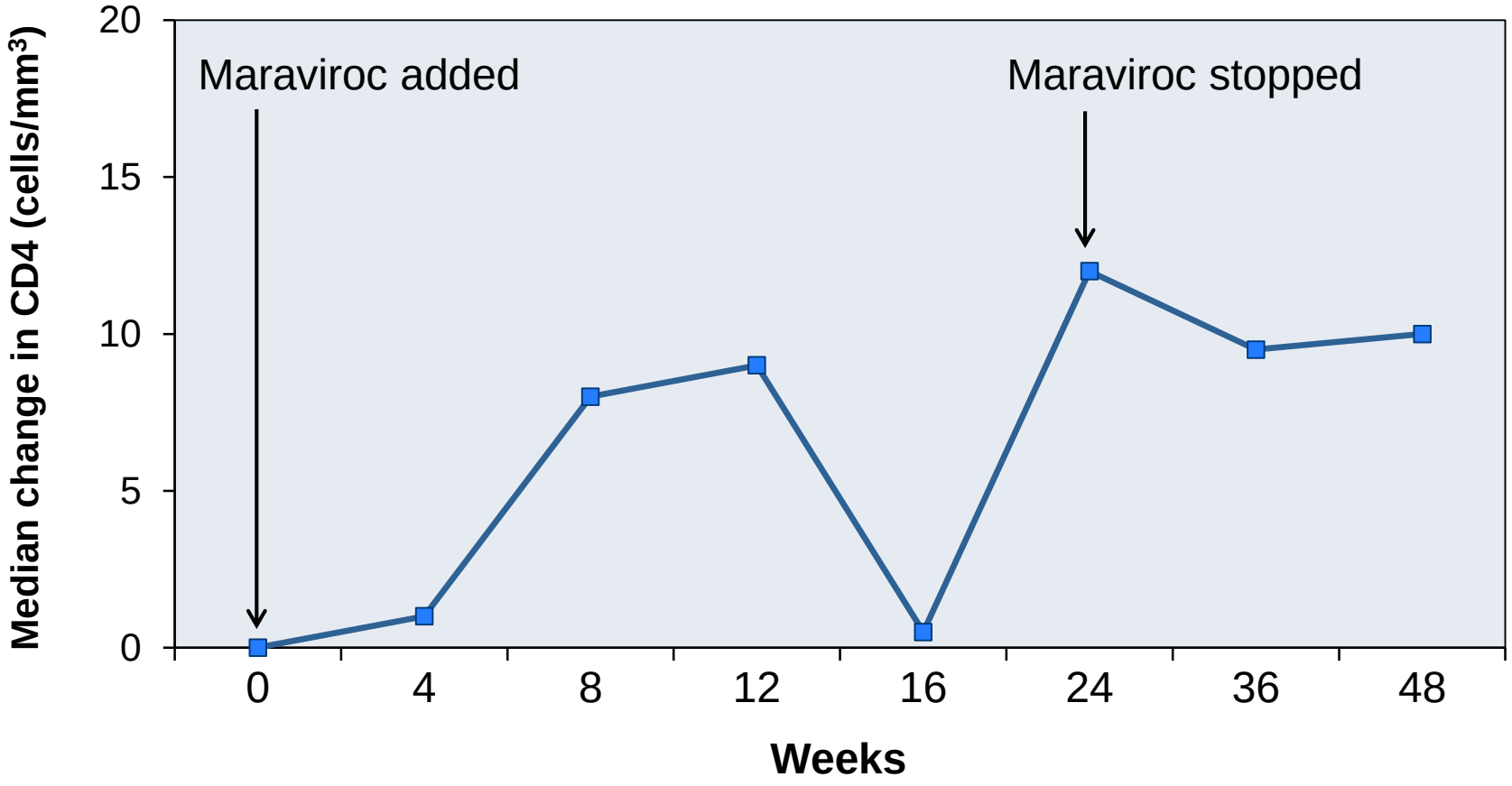
→ **MVC + Suppressive ART**
(n = 34)

Source: Wilkin TJ, et al. J Infect Dis. 2012;206:534-42.

Adding Maraviroc to Suppressive ART for Suboptimal CD4 Recovery

ACTG 5256: Results

Change in CD4 Count with Maraviroc Intensification



*The median increase in CD4(+) T-cell count from baseline to week 24 was 12 cells/mm^3.

Source: Wilkin TJ, et al. J Infect Dis. 2012;206:534-42.

Adding Maraviroc to Suppressive ART for Suboptimal CD4 Recovery
ACTG 5256: Conclusions

Conclusions: "Adding maraviroc to suppressive ART for 24 weeks was not associated with an increase in $CD4^+$ T-cell counts of at least 20 cells/mm^3. Further studies of CCR5 antagonists in the dampening of immune activation associated with HIV infection are warranted."

Source: Wilkin TJ, et al. J Infect Dis. 2012;206:534-42.

SWITCH STUDIES

Maraviroc

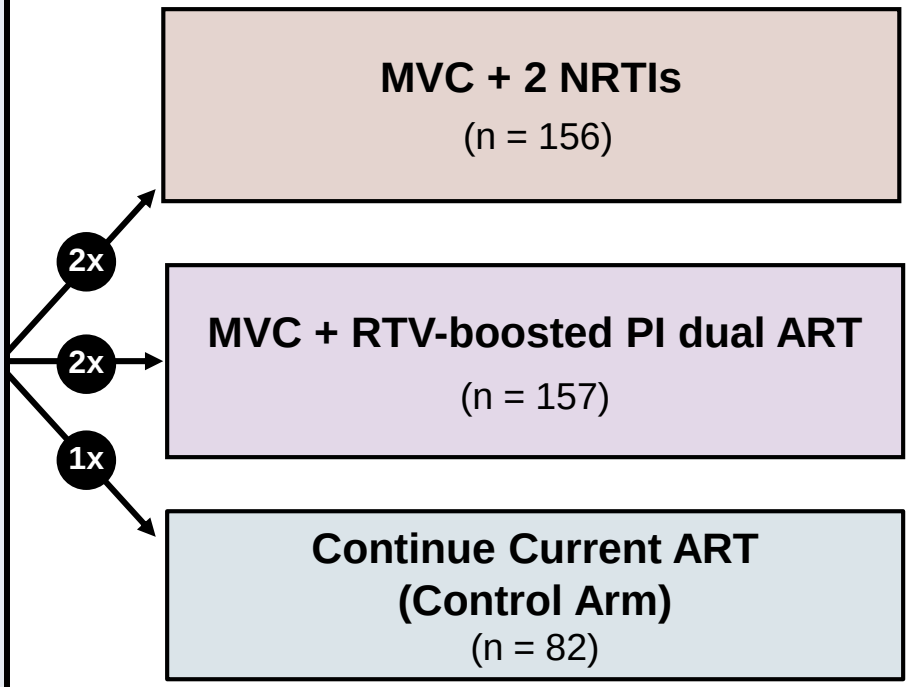
Switch from Boosted PI to Maraviroc with Suppressed HIV

MARCH

Switch from Boosted PI to Maraviroc with Suppressed HIV
MARCH: Study Design

Study Design: MARCH

- **Background**: Randomized, multicenter, open-label switch study
- **Inclusion Criteria (n = 395)**
  - Adults with HIV-1
  - R5-tropic HIV
  - HIV RNA <200 copies/mL on stable (>24 weeks) 2 NRTI + boosted PI regimen
  - Non-pregnant, not breastfeeding, no hepatitis B coinfection, no past virologic failure or resistance mutations
- **Treatment Arms**
  - Maraviroc + 2 NRTIs
  - Maraviroc + Boosted PI + dual therapy
  - Continue current ART



Source: Pett SL, et al. Clin Infect Dis. 2016;63:122-32.

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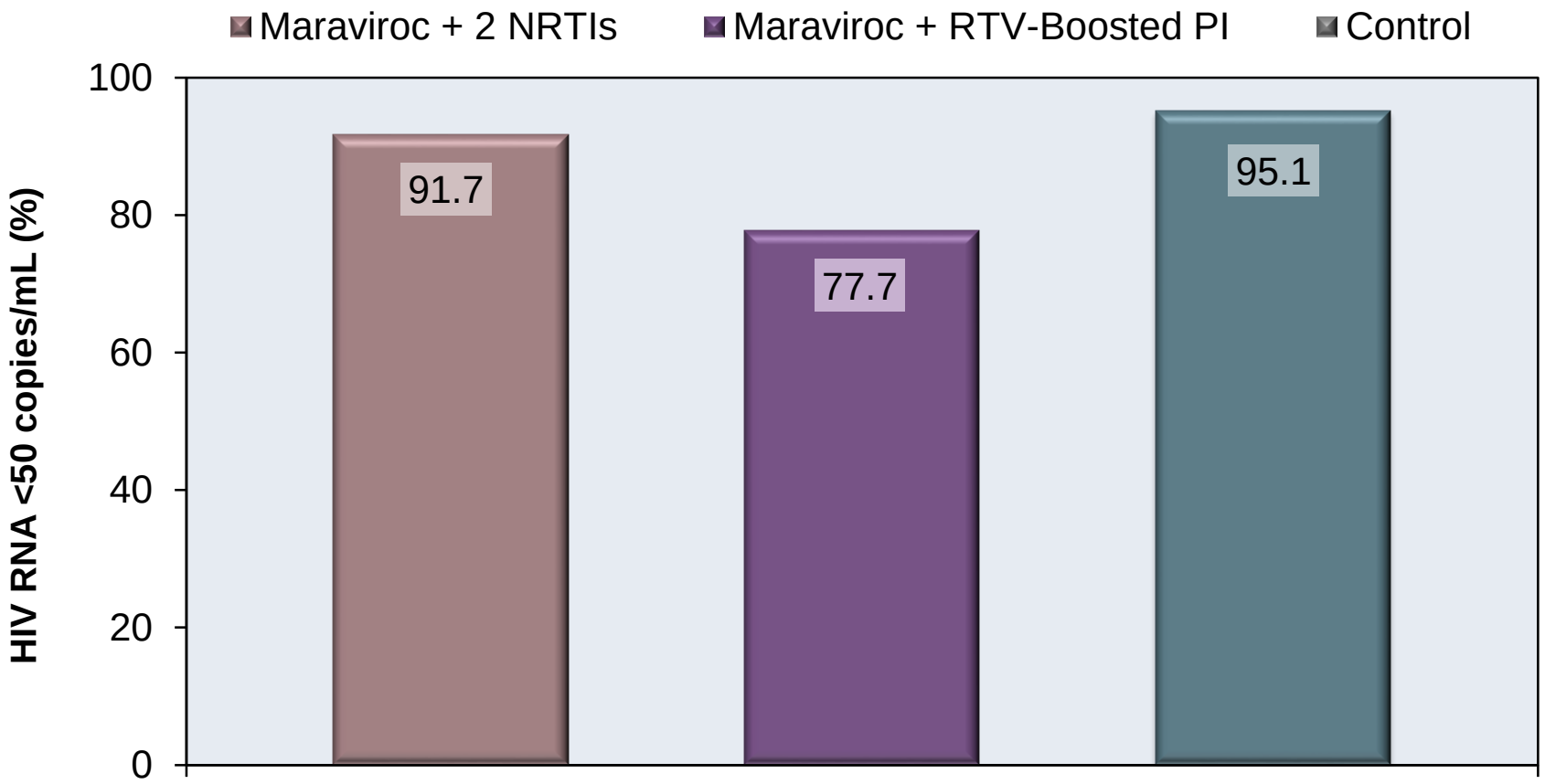
Switch from Boosted PI to Maraviroc with Suppressed HIV
MARCH: Results

Week 48 Results (Intention to Treat Analysis, ITT)



Source: Pett SL, et al. Clin Infect Dis. 2016;63:122-32.

Switch from Boosted PI to Maraviroc with Suppressed HIV
MARCH: Conclusions

Conclusions: “These data support MVC as a switch option for ritonavir-boosted PIs when partnered with a 2-N(t)RTI backbone, but not as part of N(t)RTI-sparing regimens comprising MVC with PI/r.”

Source: Pett SL, et al. Clin Infect Dis. 2016;63:122-32.

Maraviroc plus Raltegravir

ROCnROL (ANRS 157) Trial

Maraviroc + Raltegravir
ROCnRal (ANRS 157): Study Design

Study Design: ROCnRAL (ANRS 157)

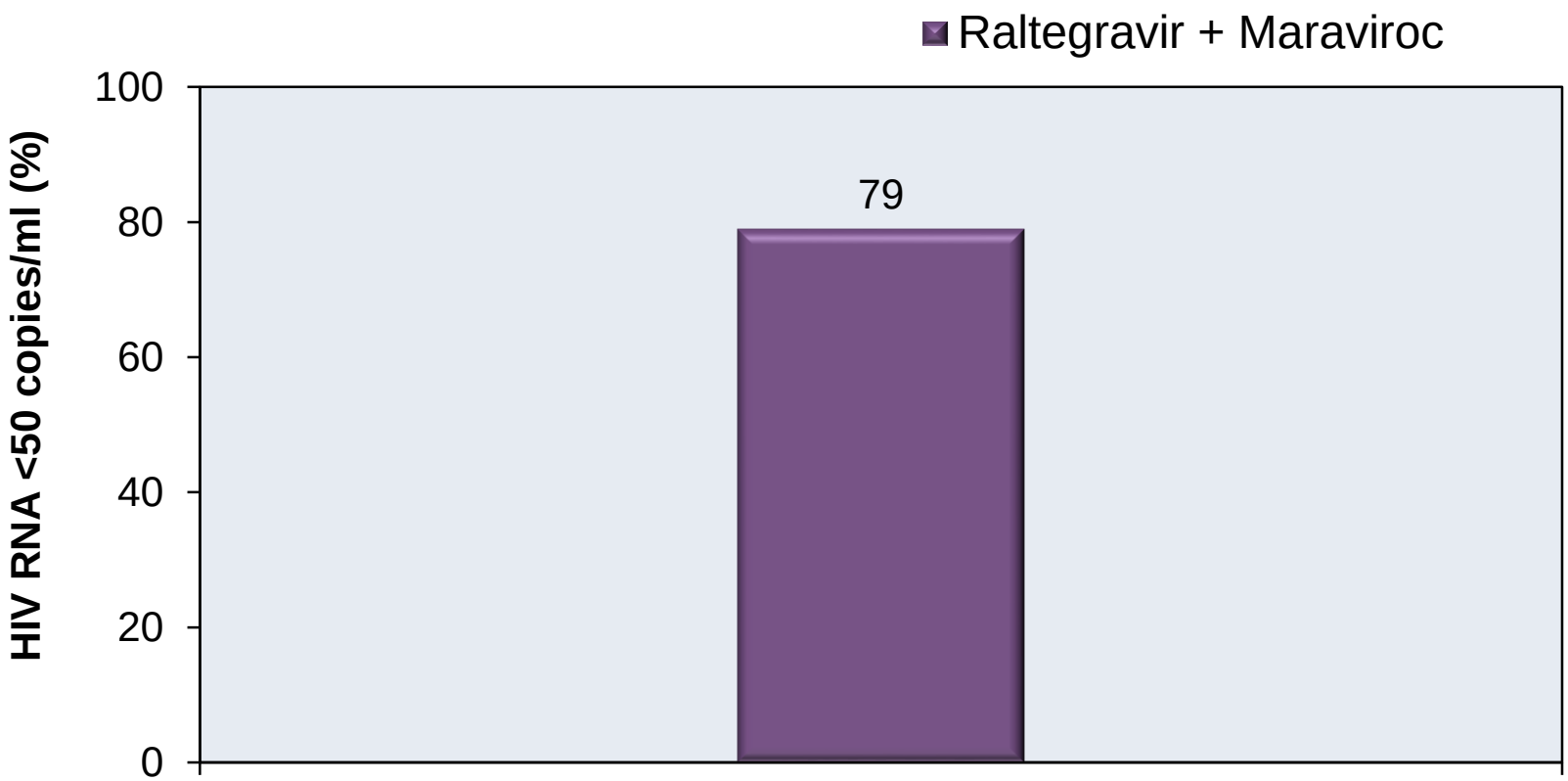
- **Background**: Pilot, phase II, single-arm trial to evaluate capacity of a dual regimen of raltegravir plus maraviroc to maintain viral suppression in virally suppressed HIV-infected patients with hyperlipidemia
- **Inclusion Criteria (n = 44)**
  - Adults
  - On ART for ≥5 years
  - Naïve to integrase inhibitors and maraviroc
  - HIV RNA <200 copies/mL ≥24 months
  - HIV RNA <50 copies/mL for ≥12 months
  - R5 tropism
- **Treatment Arm**
  - Raltegravir 400 mg BID + Maraviroc 300 mg BID

→ **Raltegravir 400 mg BID + Maraviroc 300 mg BID** (n = 44)

Source: Katlama C, et al. J Antimicrob Chemother. 2014;69:1648-52.

Maraviroc + Raltegravir
ROCnRal (ANRS 157): Result

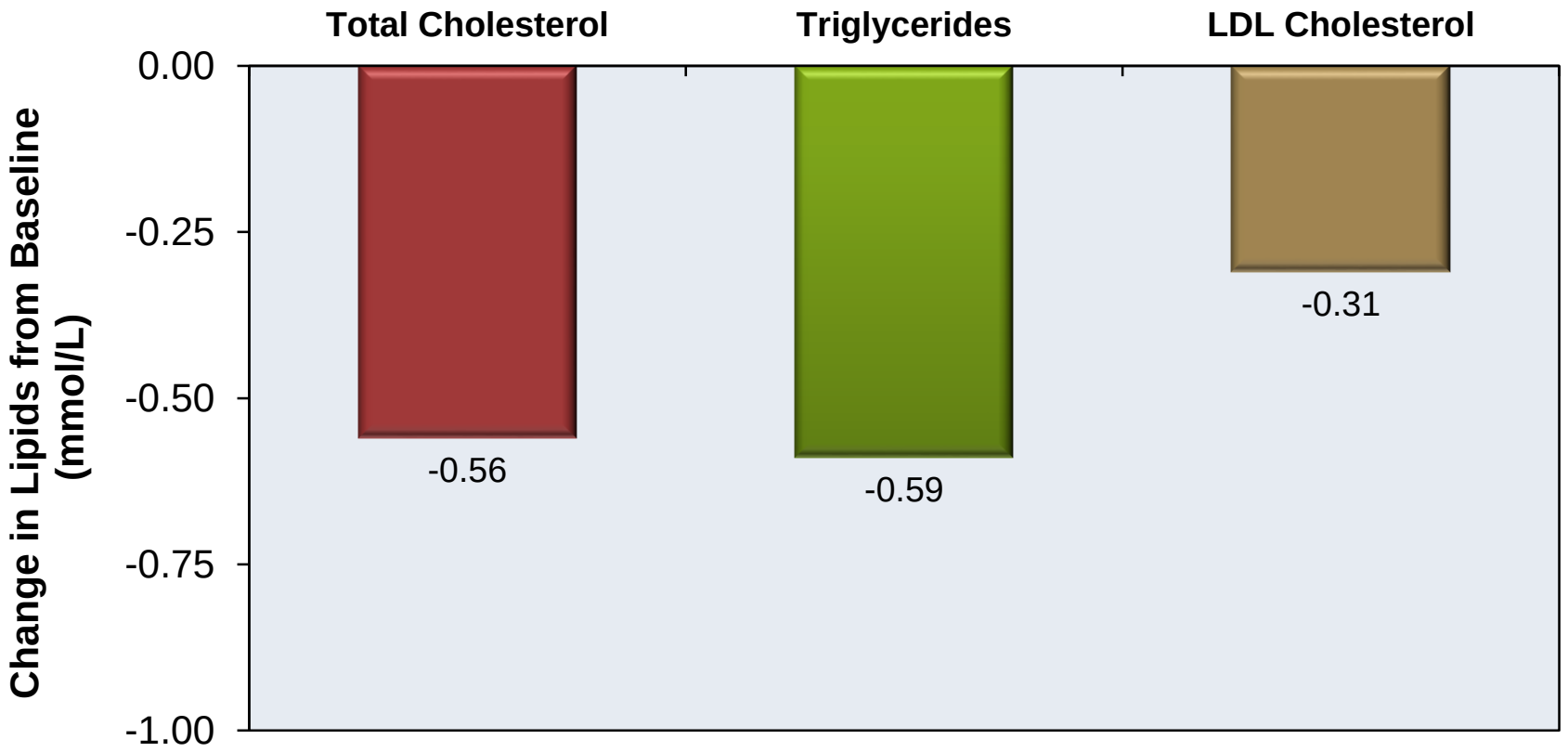
Week 24 Virologic Response



Source: Katlama C, et al. J Antimicrob Chemother. 2014;69:1648-52.

Maraviroc + Raltegravir
ROCnRal (ANRS 157): Result

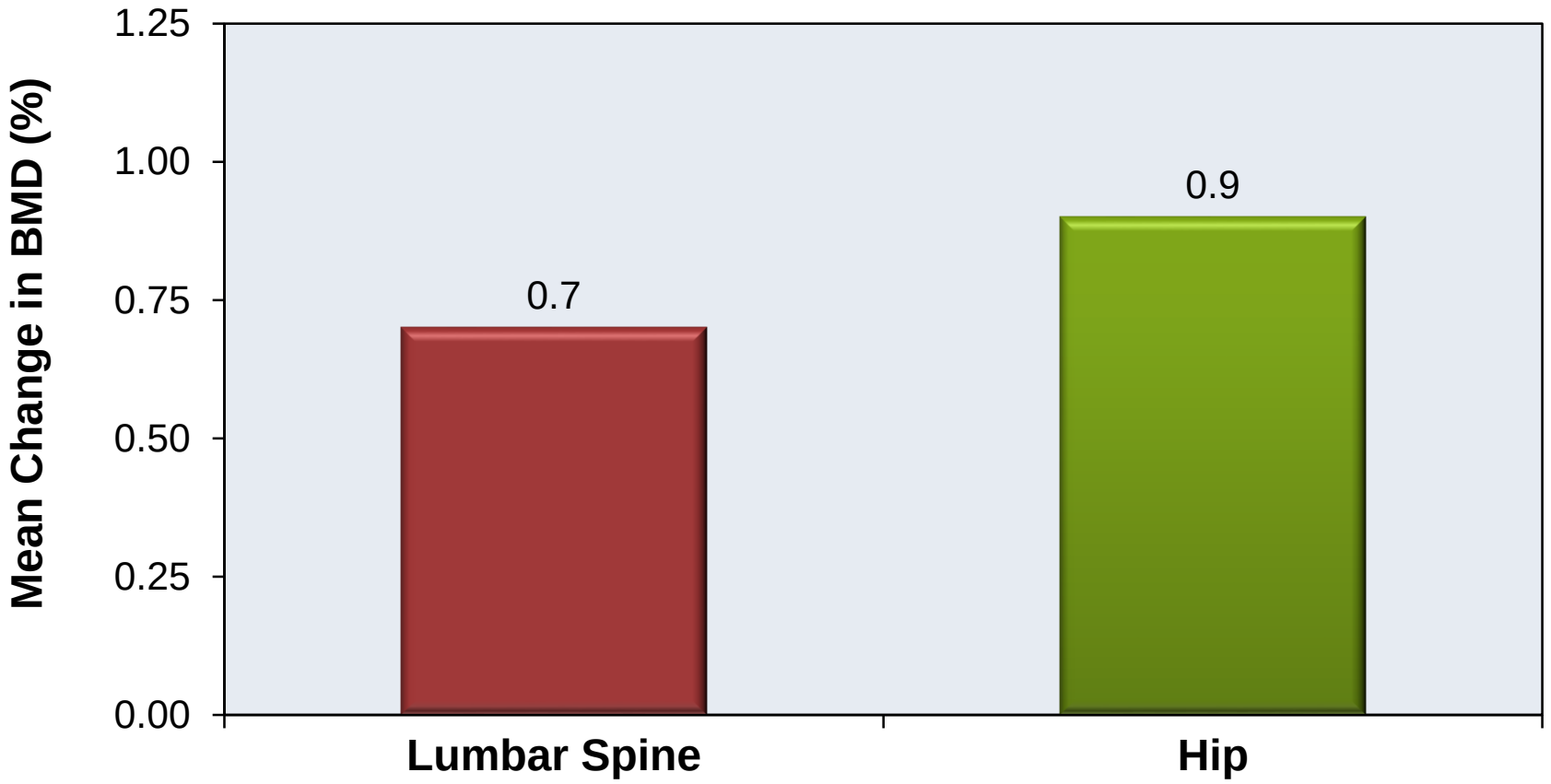
Analysis of Lipids on Dual Therapy (Median time = 19.4 weeks)



Source: Katlama C, et al. J Antimicrob Chemother. 2014;69:1648-52.

Maraviroc + Raltegravir
ROCnRal (ANRS 157): Result

Change in Bone Mineral Density from Baseline (Median interval: 26 wks)



Source: Katlama C, et al. J Antimicrob Chemother. 2014;69:1648-52.

Dual Therapy with Raltegravir plus Maraviroc in Patients Receiving Suppressive ART who have Lipohypertrophy

ROCnRAL (ANRS 157): Result

Details of Virologic Failures & Discontinuations due to Adverse Events				
Patient	HIV RNA at Failure (copies/mL)	Integrase Resistance Mutations	Tropism at Failure	Side Effects
1	2,973	None	CCR5	
2	1,453	Y143H	CXCR4	
3	8,070	N155H	CXCR4	
4	259	None	CCR5	
5	2,820	F121Y	CCR5	
6				HBV reactivation, AST/ALT >20x ULN
7				Cutaneous rash and diarrhea, possibly related to study drugs

Maraviroc + Raltegravir

ROCnRal (ANRS 157): Conclusions

Conclusions: “In long-term-experienced patients, maraviroc/raltegravir therapy lacks virological robustness despite a benefit in lipid profile and bone density.”

Source: Katlama C, et al. J Antimicrob Chemother. 2014;69:1648-52.

PREEXPOSURE PROPHYLAXIS

Maraviroc

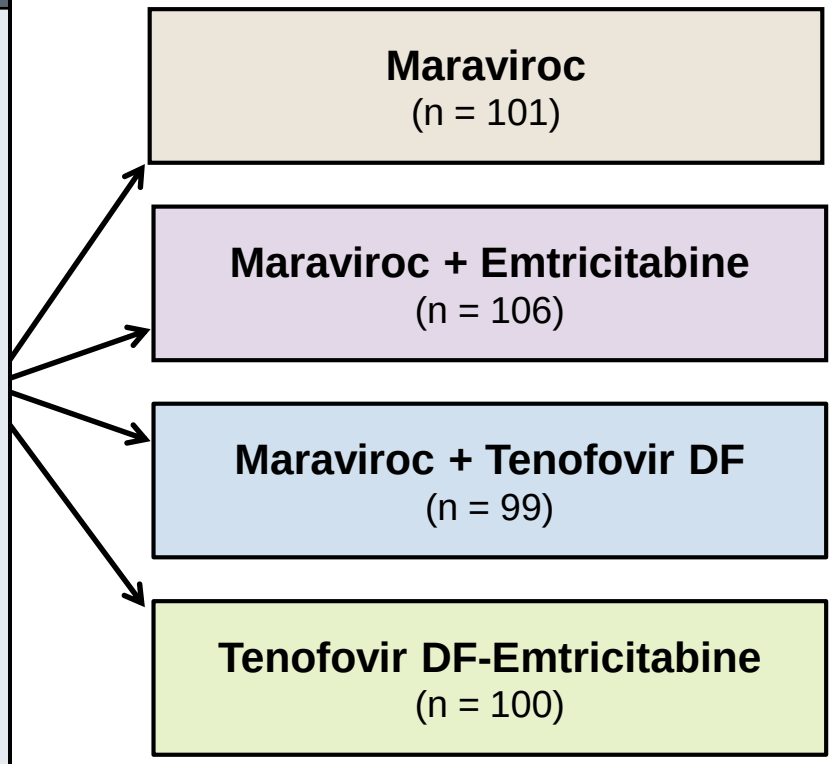
Maraviroc +/- FTC or TDF for Preexposure Prophylaxis

HPTN 069/ACTG 5305

Maraviroc +/- FTC or TDF for Preexposure Prophylaxis
HPTN 069/ACTG 5305: Study Design

Study Design: HPTN 069/ACTG 5305

- **Background**: Phase 2b, randomized, double-blind study of the safety and tolerability of maraviroc (alone or combined with FTC or TDF) for preexposure prophylaxis (PrEP), as compared to TDF-FTC, for at-risk men and transgender women
- **Inclusion Criteria (n = 406)**
  - Men and transgender women who have sex with men who self-reported condomless anal sex with at least one man within last 90 days
  - Creatinine clearance ≥70 mL/min
  - Negative HIV Ag/Ab and RNA
  - Negative hepatitis B surface Ag
  - No reported injection-drug use



Source: Gulick RM, et al. J Infect Dis. 2017;215:238-46.

Maraviroc +/- FTC or TDF for Preexposure Prophylaxis
HPTN 069/ACTG 5305: Results

HPTN 069/ACTG 5305: Adverse Events (AE's) at Week 48 ITT Analysis

	MVC (n = 101)	MVC + FTC (n = 106)	MVC + TDF (n = 99)	TDF-FTC (n = 100)
Permanent study drug discontinuation	7 (7%)	9 (9%)	12 (12%)	8 (8%)
Time to permanent discontinuation, median days (IQR)	120 (74-263)	66 (42-222)	113 (42-260)	67 (34-141)
Grade 3-4 AE's, # of participants, # of events	13, 15	11, 15	11, 14	20, 23
Grade 3-4 AE's, adverse event rate per person-year	0.17	0.16	0.17	0.19

Number discontinuing and time to discontinuation did not differ among study regimens (P = .60).
Rates of grade 3–4 adverse events did not differ among regimens (P = .37).

Source: Gulick RM, et al. J Infect Dis. 2017;215:238-46.

Maraviroc +/- FTC or TDF for Preexposure Prophylaxis
HPTN 069/ACTG 5305: Results

Week 48 Results (Intention to Treat Analysis, ITT)

HIV Infections that Occurred During the HPTN 069/ACTG 5305 study

	Age	HIV Risk Group	Study Arm	1st Reactive HIV Test, Study Week	HIV RNA, copies/mL	HIV Tropism	Genotypic Drug Resistance	Study drug concentration at seroconverstion visit, ng/mL
1	20	MSM	MVC + TDF	9	122,150	R5	None	MVC: 0 TFV: 0
2	61	MSM	MVC	16	981	R5	None	MVC: 145
3	21	MSM	MVC	28	106,240	R5	None	MVC: 0
4	35	MSM	MVC	38	13,626	R5	None	MVC: 6.7
5	36	MSM	MVC	48	52,191	R5	None	MVC: 0.7

Source: Gulick RM, et al. J Infect Dis. 2017;215:238-46.

Maraviroc +/- FTC or TDF for Preexposure Prophylaxis
HPTN 069/ACTG 5305: Conclusions

Conclusions: “MVC-containing regimens were safe and well tolerated compared with TDF + FTC; this study was not powered for efficacy. Among those acquiring HIV infection, drug concentrations were absent, low, or variable. MVC-containing regimens may warrant further study for pre-exposure prophylaxis..”

Source: Gulick RM, et al. J Infect Dis. 2017;215:238-46.

Acknowledgment

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National HIV Curriculum

AETC AIDS Education & Training Center Program