

# A Multicenter, Randomized, Double-Blind, Comparative Trial of a Novel CCR5 Antagonist, Maraviroc Versus Efavirenz, both in Combination with Combivir (Zidovudine/Lamivudine), for the Treatment of Antiretroviral-Naive Subjects Infected with R5 HIV 1: Week 48 Results of the MERIT Study

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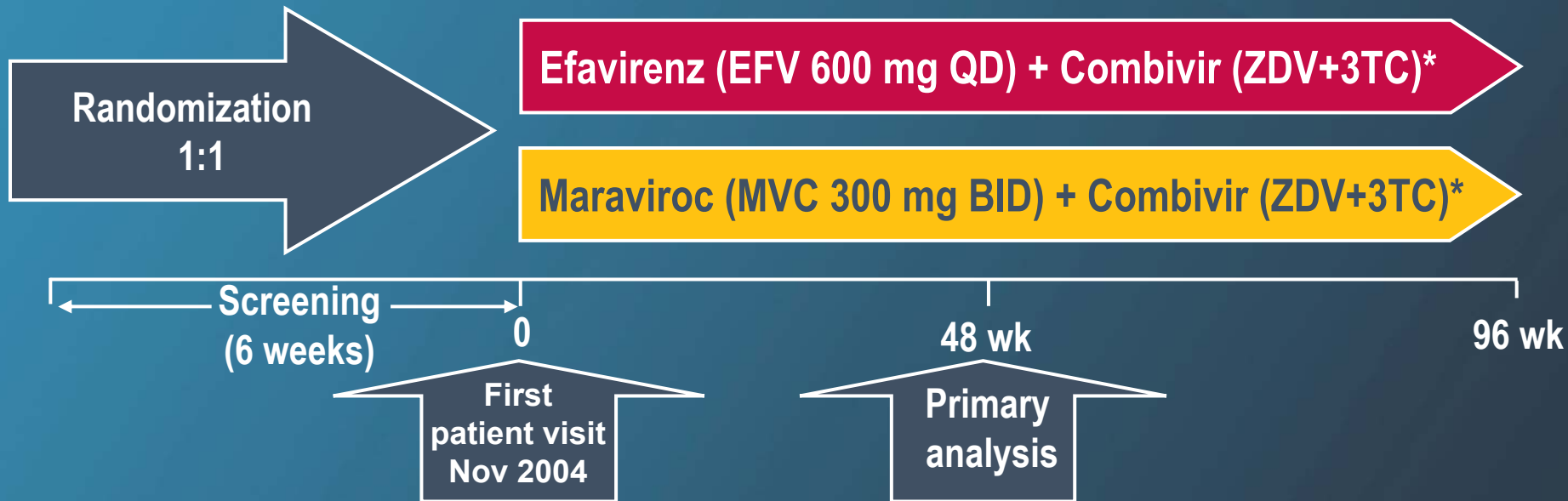
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# MERIT Study: Phase 3 Trial Design



## Patient eligibility criteria:

- $\geq 16$  years of age
- HIV-1 RNA  $\geq 2,000$  copies/mL
- Treatment naive
- No evidence of resistance to EFV, ZDV, or 3TC
- R5 HIV-1 infection

## Patients stratified by:

- HIV-1 RNA  $<$  and  $\geq 100,000$  copies/mL at screening
- Geographic location: Northern Hemisphere and Southern Hemisphere

MVC QD arm discontinued at end of Phase 2b (week 16) for failure to meet protocol-defined criteria to continue (205 pts completed 16 weeks)

\*Patients experiencing toxicity to ZDV or 3TC were permitted to substitute an alternative NRTI

# Demographics and Baseline Characteristics

Randomized: N=740 Treated: N=721	EFV + CBV N=361	MVC + CBV N=360
Mean age, yrs (range)	37.4 (18–77)	36.7 (20–69)
Male, n (%)	259 (71.7)	256 (71.1)
Race, n (%)		
White	198 (54.8)	204 (56.7)
Black	133 (36.8)	123 (34.2)
Asian	5 (1.4)	6 (1.7)
Other	25 (6.9)	27 (7.5)
Median CD4+ count, cells/mm <sup>3</sup> (range)	254 (8–1,053)	241 (5–1,422)
Mean HIV-1 RNA, log <sub>10</sub> copies/mL (SD)	4.88 (0.699)	4.86 (0.640)

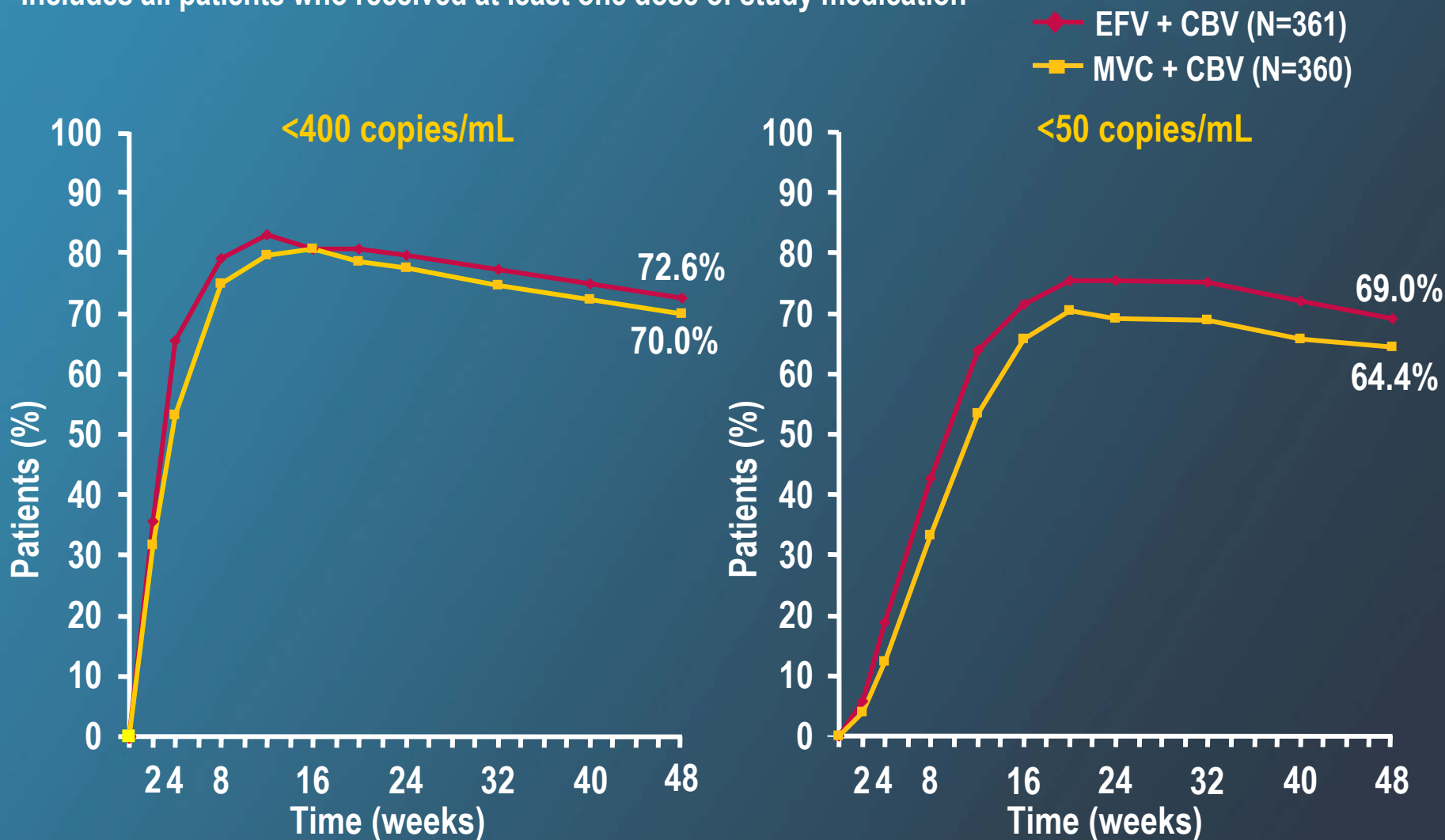
# Summary of Discontinuations Through 48 Weeks

Includes all patients who received at least one dose of study medication

Reason for discontinuation	EFV + CBV N=361	MVC + CBV N=360
All, n (%)	91 (25.2)	97 (26.9)
Adverse event, n (%)	49 (13.6)	15 (4.2)
Lack of efficacy, n (%)	15 (4.2)	43 (11.9)
Other reason, n (%)	9 (2.5)	14 (3.9)
Withdrew consent or lost to follow-up, n (%)	18 (5.0)	25 (6.9)

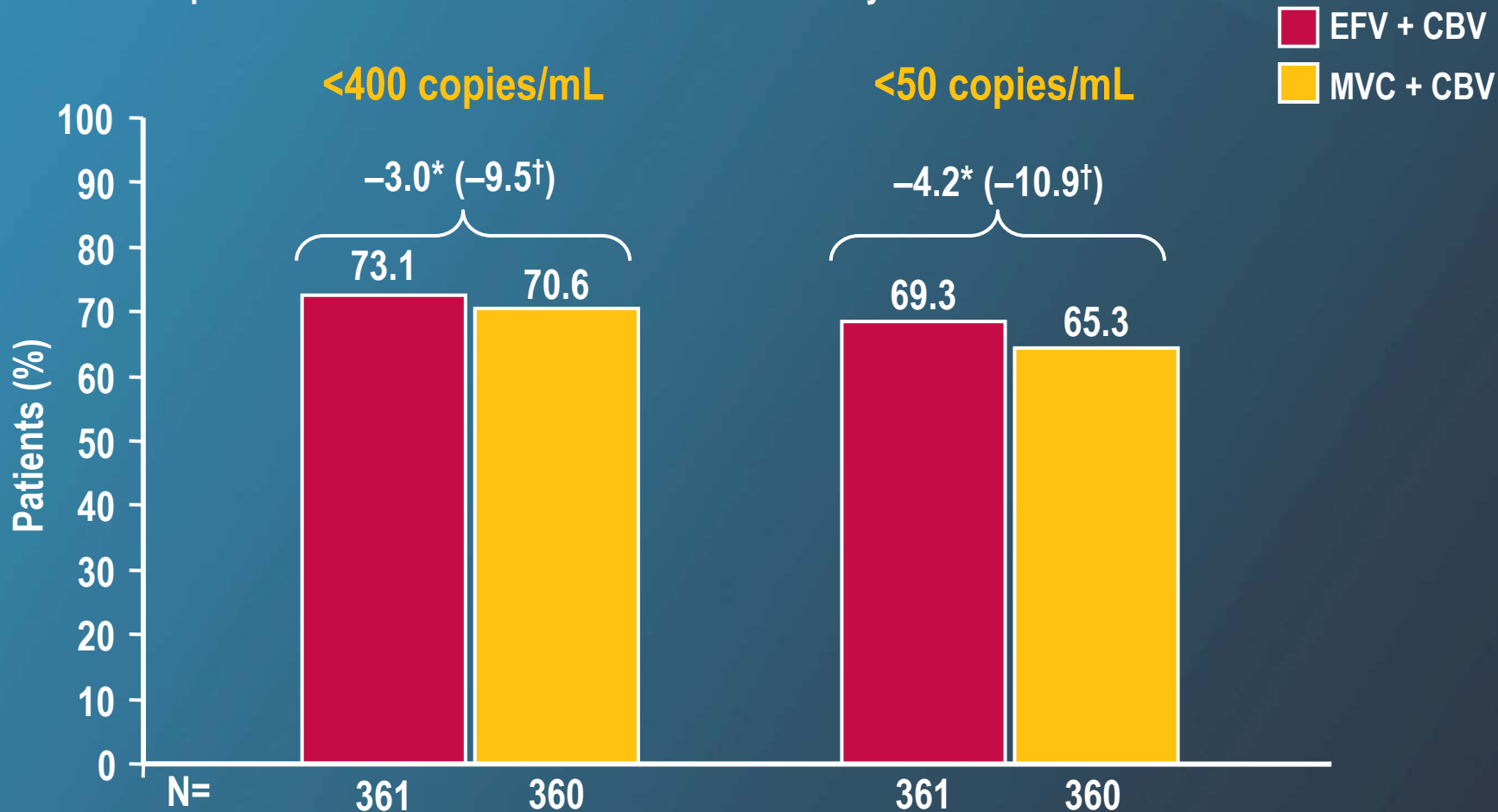
# Percentage of Patients with Undetectable HIV-1 RNA by Visit

Includes all patients who received at least one dose of study medication



# Percentage of Patients with Undetectable HIV-1 RNA at Week 48 (Primary Endpoint)

Includes all patients who received at least one dose of study medication



\*Difference (adjusted for randomization strata)

†Lower bound of 1-sided 97.5% confidence interval; noninferiority margin = -10%

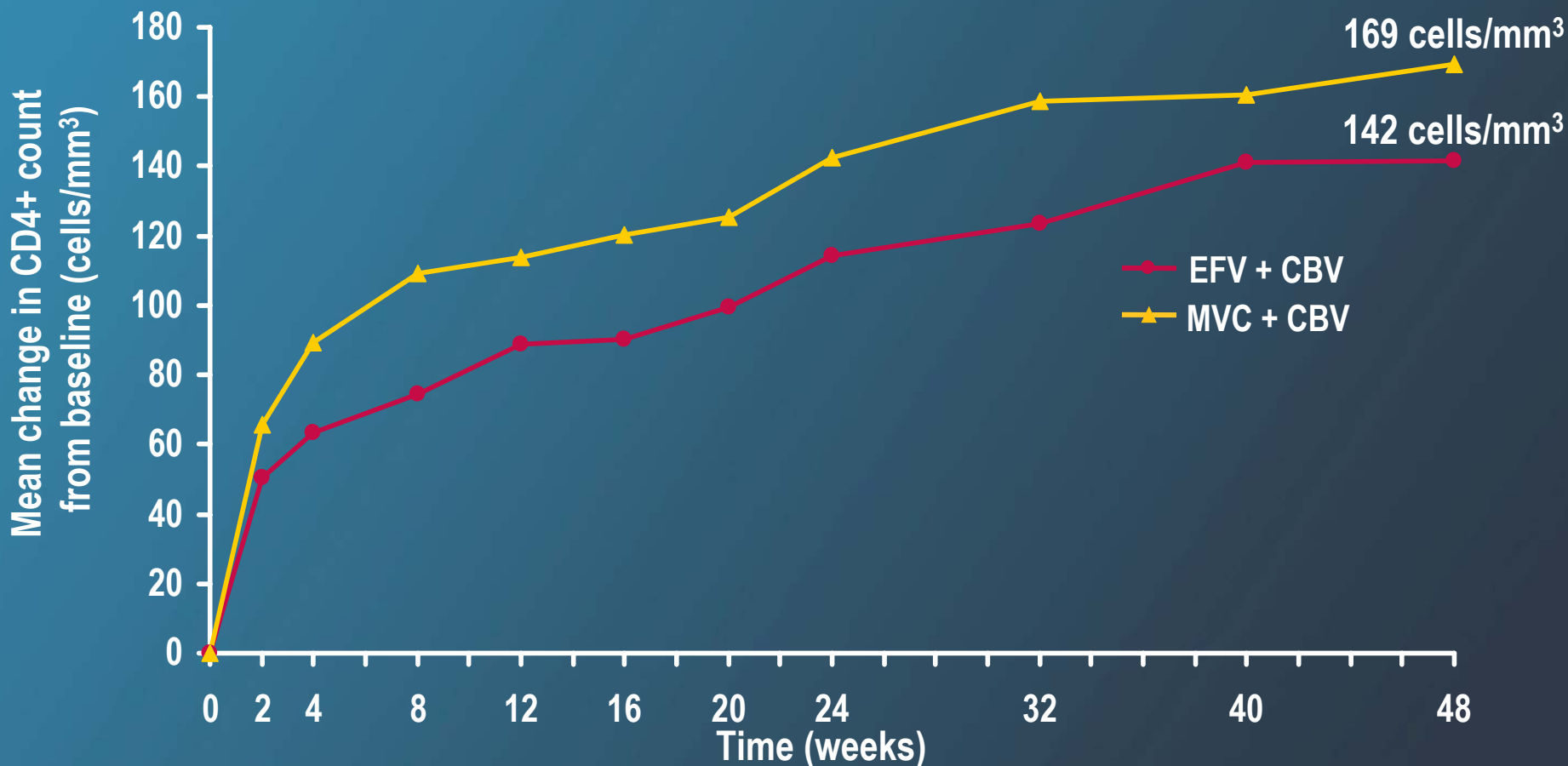
Per-protocol analysis: <400 copies/mL difference = -4.1 (-10.5†), <50 copies/mL difference = -4.4 (-11.2†)

MERIT Study 48 weeks

Intent-to-treat (ITT) analysis

# Mean Change in CD4+ Count from Baseline by Visit

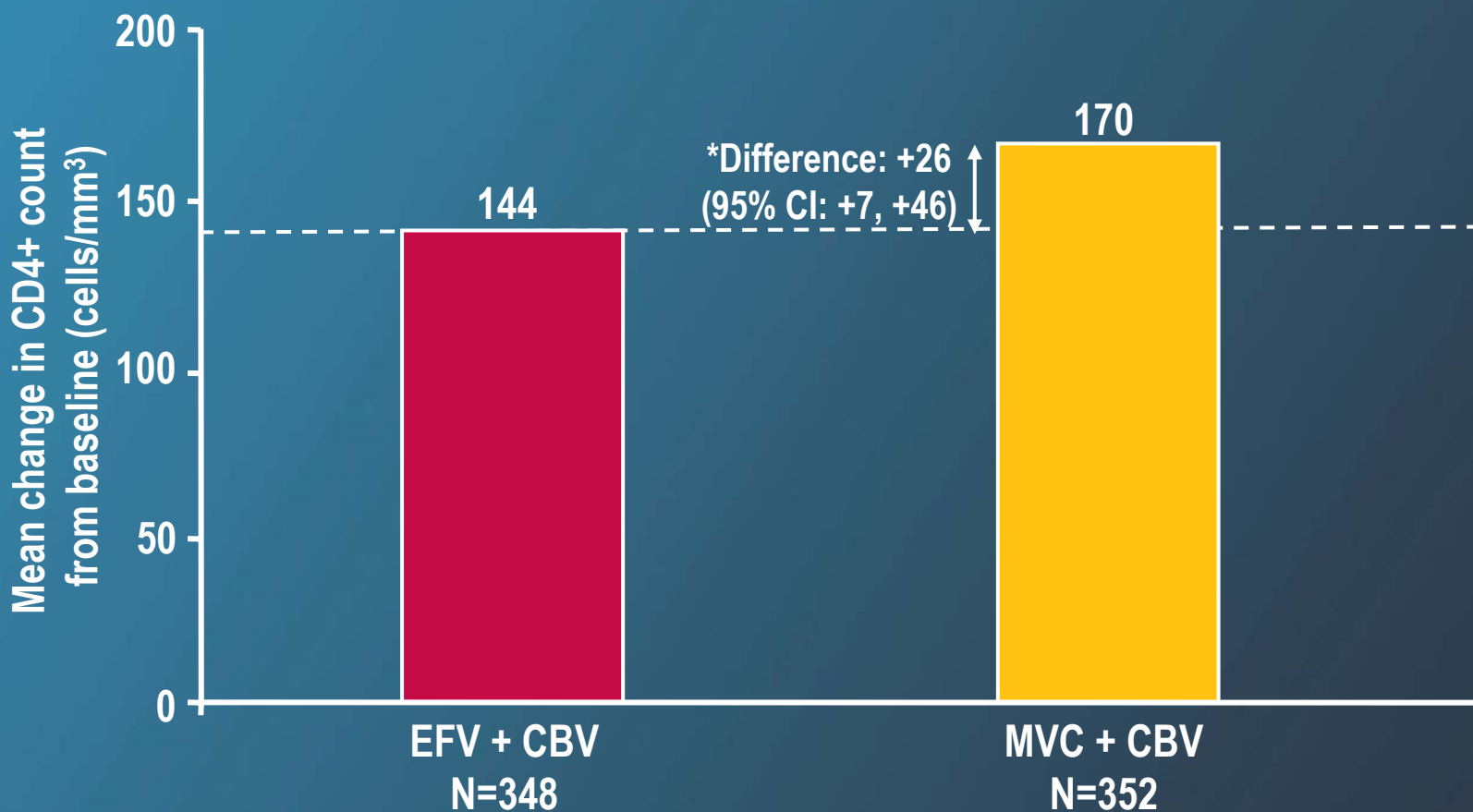
Includes all patients who received at least one dose of study medication



N =	331	346	348	348	348	348	348	348	348	348
N =	336	350	351	352	352	352	352	352	352	352

# Mean Change in CD4+ Count from Baseline to Week 48

Includes all patients who received at least one dose of study medication



\* Difference adjusted for randomization strata

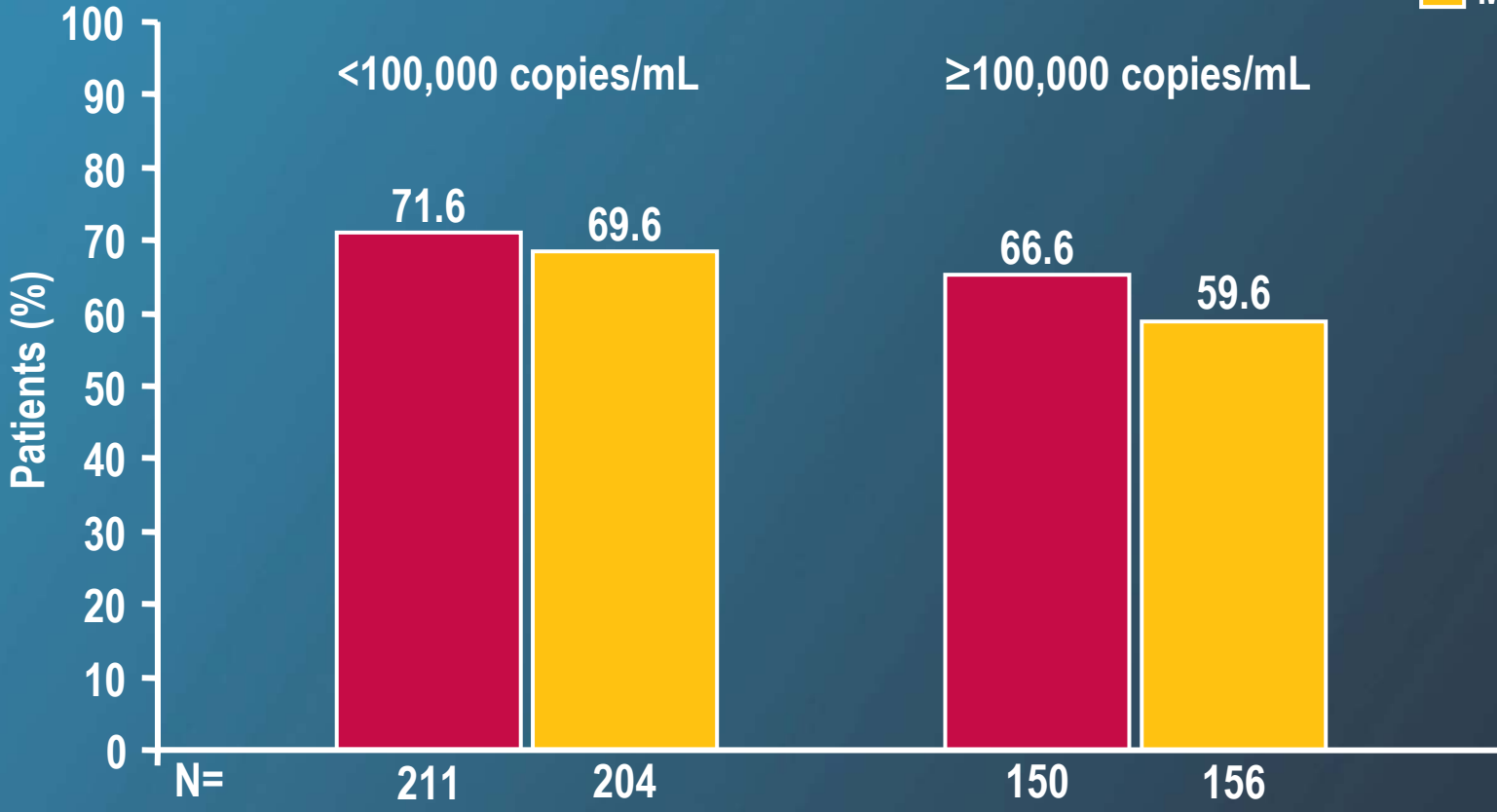
MERIT Study 48 weeks

LOCF

# Percentage of Patients with HIV-1 RNA <50 copies/mL by HIV-1 RNA at Screening

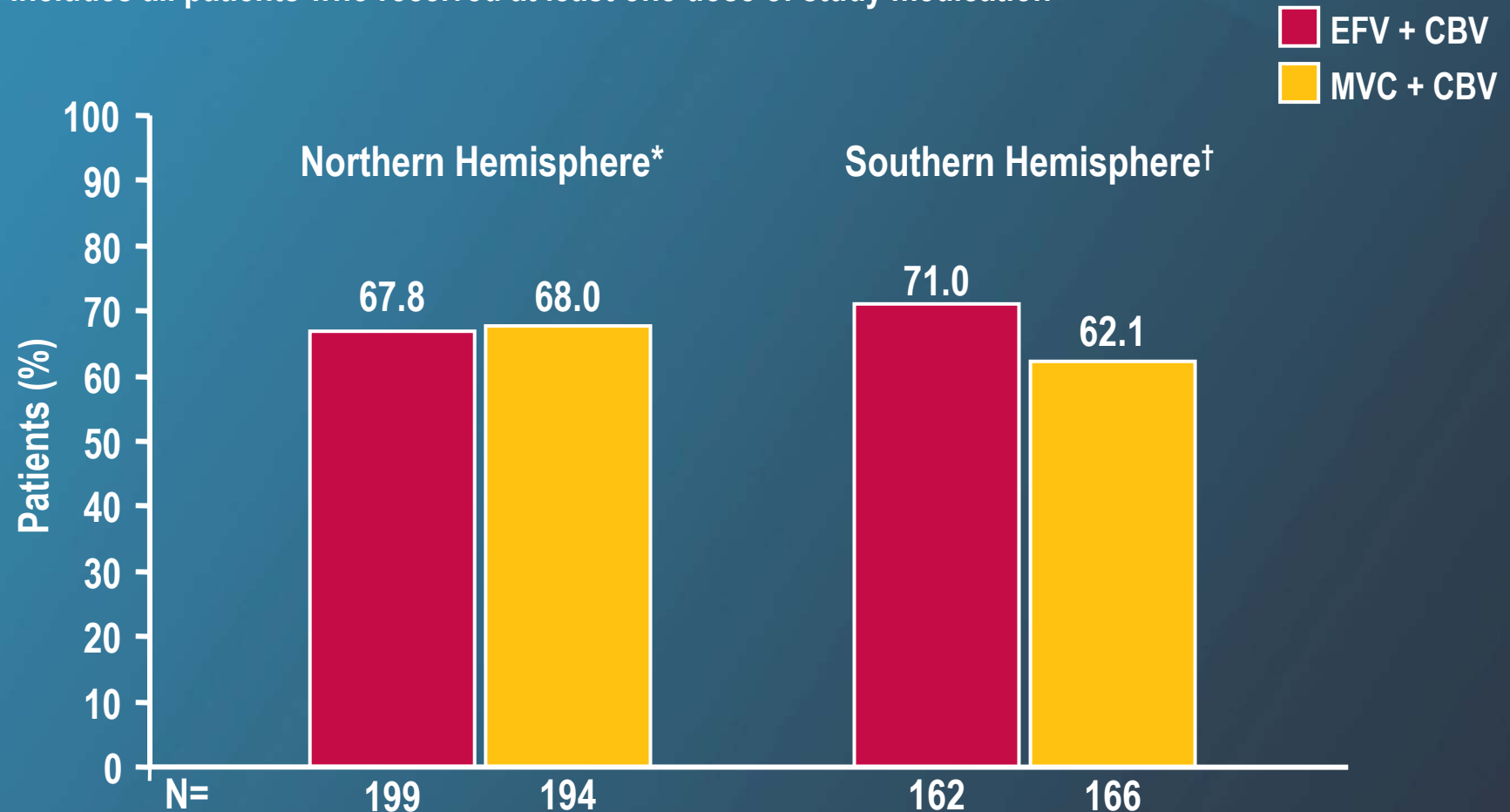
Includes all patients who received at least one dose of study medication

EFV + CBV  
MVC + CBV



# Percentage of Patients with HIV-1 RNA <50 copies/mL by Geographic Region

Includes all patients who received at least one dose of study medication



\*Patients at study centers in North America and Europe

†Patients at study centers in Argentina, South Africa and Australia

# Safety Analyses

Includes all patients who received at least one dose of study medication

All causalities and severities	EFV + CBV N=361	MVC + CBV N=360
Patients with adverse events	340 (94.2)	331 (91.9)
Patients with grade 3 AEs, n (%)	66 (18.3)	51 (14.2)
Patients with grade 4 AEs, n (%)	24 (6.6)	22 (6.1)
Patients with SAEs, n (%) <sup>†</sup>	46 (12.7)	41 (11.3)
Patients with Category C events, n (%)	12 (3.3)	6 (1.7)
Malignancies	16 (4.4)	10 (2.8)
Deaths <sup>†*</sup> , n (%)	1	1

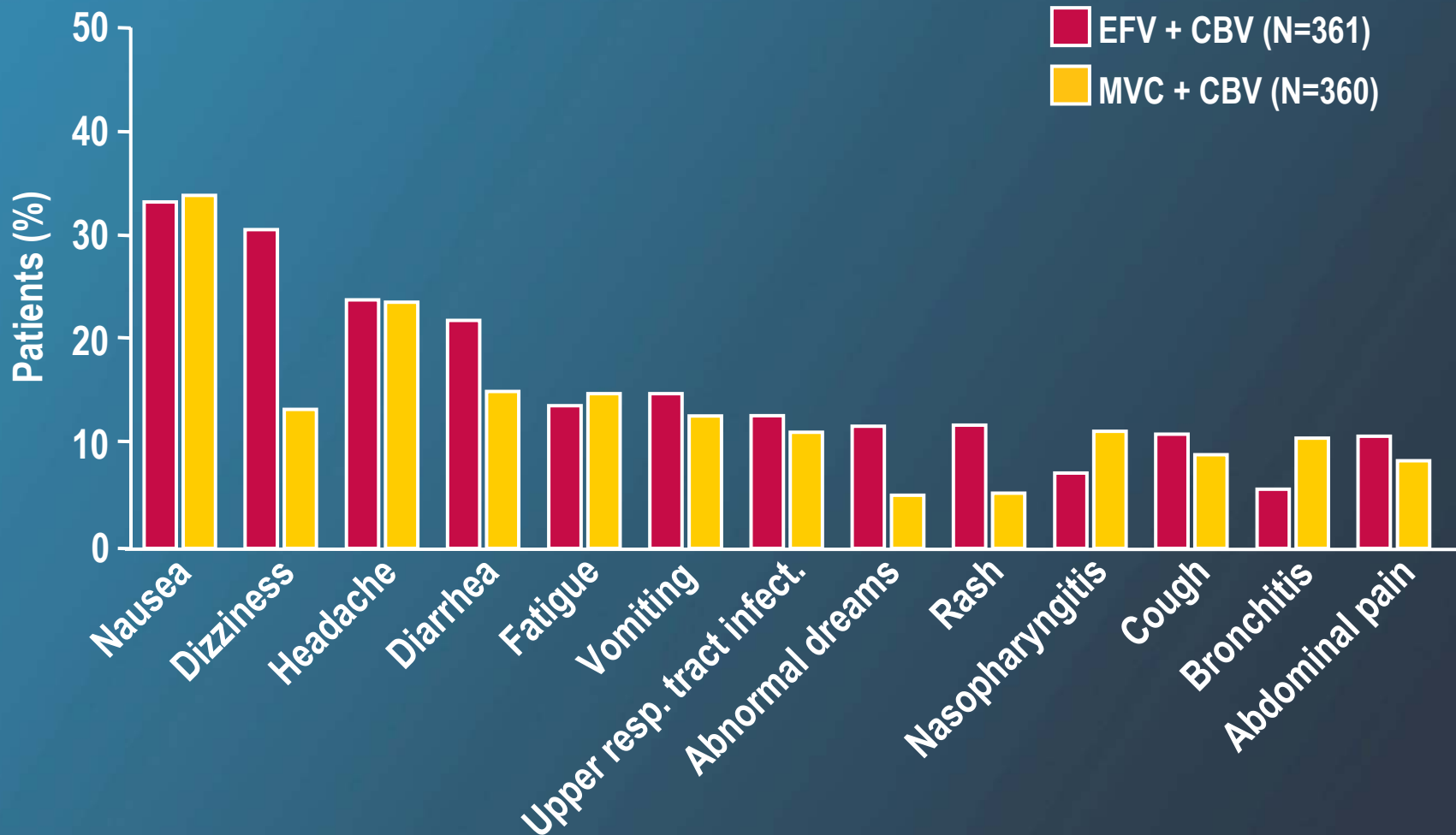
AEs = adverse events; SAEs = serious adverse events

<sup>†</sup>Based on all data through 21 June 2007

\*Deaths reported up to 28 days after stopping study drug; one additional death on EFV within 28 days, date of death not captured in database

# Incidence of Adverse Events Occurring in $\geq 10\%$ of Patients in Any Group, Unadjusted for Exposure

Includes all patients who received at least one dose of study medication

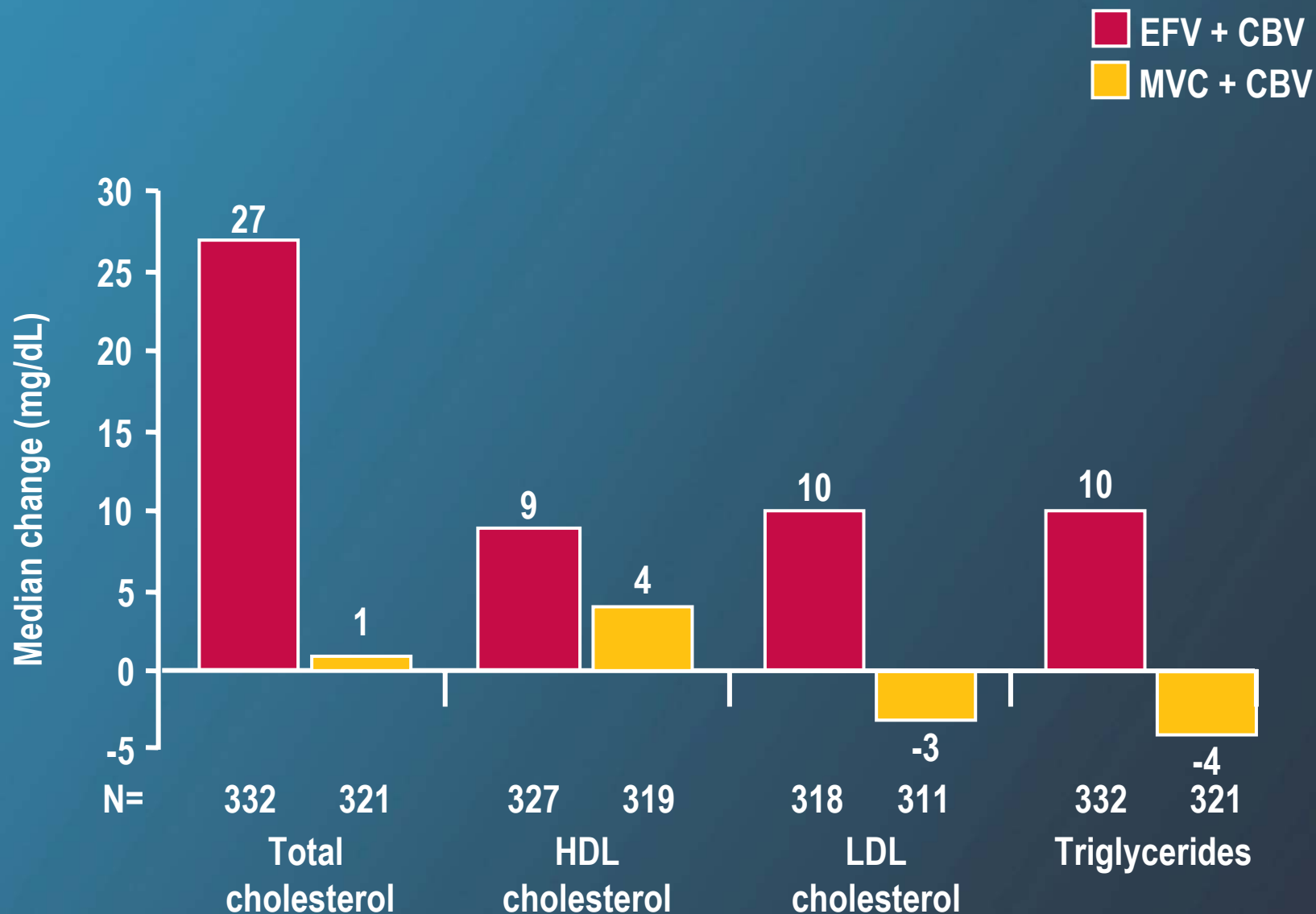


# Incidence of Category C AIDS-Defining Events

Includes all patients who received at least one dose of study medication

Number of patients	EFV + CBV N=361	MVC + CBV N=360
Category C events	12 (3.3)	6 (1.7)
<b>Infections</b>	<b>8 (2.2)</b>	<b>5 (1.4)</b>
Tuberculosis	8	1
Herpes simplex	1	1
Lobar pneumonia/Lower respiratory tract infection	0	2
<i>Pneumocystis jiroveci</i> pneumonia	0	1
<b>Malignancies</b>	<b>4 (1.1)</b>	<b>1 (0.3)</b>
Hodgkin's disease	2	0
NHL/Diffuse large B-cell lymphoma	1	1
Kaposi's sarcoma	1	0

# Median Maximum Change in Fasting Lipids



# Proportion of Patients with Grade 3 or 4 Liver Function Test Values Without Regard to Baseline

All causalities, n (%) Unadjusted for duration of exposure	EFV + CBV	MVC + CBV
<b>AST:</b> Grade 3 >5.0 to 10.0 ULN* Grade 4 >10.0 x ULN*	9/350 (2.6%) 2/350 (0.6%)	7/353 (2.0%) 5/353 (1.4%)
<b>ALT:</b> Grade 3 >5.0 to 10.0 ULN* Grade 4 >10.0 x ULN*	9/350 (2.6%) 2/350 (0.6%)	9/353 (2.5%) 2/353 (0.6%)
<b>Total bilirubin:</b> Grade 3 >2.5 to 5.0 x ULN* Grade 4 >5.0 x ULN*	0/345 0/345	3/352 (0.9%) <sup>†</sup> 0/352

\*Upper limit of normal

<sup>†</sup>All three patients had hyperbilirubinemia not associated with transaminase elevations, two associated with Gilbert's syndrome.

# Summary of 48-Week Primary Analyses (1)

- The percentage of subjects discontinuing from the study prior to Week 48 was similar in the MVC (26.9%) and EFV (25.2%) arms
  - The rate of discontinuation due to lack of efficacy was higher with MVC (11.9%) than with EFV (4.2%)
  - The rate of discontinuation due to adverse events was lower with MVC (4.2%) than with EFV (13.6%)
- Based on the pre-planned statistical analysis (noninferiority margin of –10%), MVC was:
  - Noninferior to EFV based on <400 copies/mL endpoint (70.6% vs 73.1%)
  - But not the <50 copies/mL endpoint (65.3% vs 69.3%)
- CD4+ cell count increases were higher in patients receiving MVC compared to EFV (+170 vs +144 cells/mm<sup>3</sup>)

## Summary of 48-Week Primary Analyses (2)

- Fewer patients experienced grade 3 or 4 adverse events in the MVC arm than in the EFV arm
- Fewer patients experienced Category C events in the MVC arm (n=6) than in the EFV arm (n=12)
  - The incidence of AIDS-defining malignancies and malignancies in general was lower in the MVC arm than in the EFV arm
- Grade 3/4 transaminase elevations were infrequent and occurred at a similar rate in the two treatment arms
- Median lipid increases from baseline were greater in the EFV arm

# Acknowledgements

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- Patients participating in the MERIT study
- Investigators and study site staff
- Pfizer MERIT study team
- Monogram Biosciences