National HIV Curriculum

Dolutegravir-Lamivudine (*Dovato*)

Prepared by:

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Last Updated: November 28, 2022

Dolutegravir-Lamivudine

Dolutegravir-Lamivudine

50 mg → INSTI

300 mg → NRTI

Dose: 1 tablet once daily with or without food

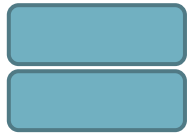
Photograph courtesy of ViiV

Dolutegravir-Lamivudine

- **Indication**
  - Complete regimen for the treatment of HIV-1 (initial or maintenance ART) for adults or adolescents 12 years or older weighing at least 40 kg
  - Insufficient data for use in pregnancy
- **Class**
  - Dolutegravir: integrase strand transfer inhibitor (INSTI)
  - Lamivudine: nucleoside reverse transcriptase inhibitor (NRTI)
- **Dosing**
  - Fixed dose tablet: Dolutegravir 50 mg and Lamivudine 300 mg
  - 1 tablet once daily, with or without food
  - Not recommended in patients with renal impairment
  - Not recommended in patients with severe hepatic impairment (Child-Pugh C)
- **Common Adverse Effects** (≥2%)
  - Headache, nausea, diarrhea, insomnia, fatigue, anxiety, and dizziness

Dolutegravir-Lamivudine: **Initial Antiretroviral Therapy**

Initial Antiretroviral Therapy
Dolutegravir-Lamivudine (2-Drug Regimen)

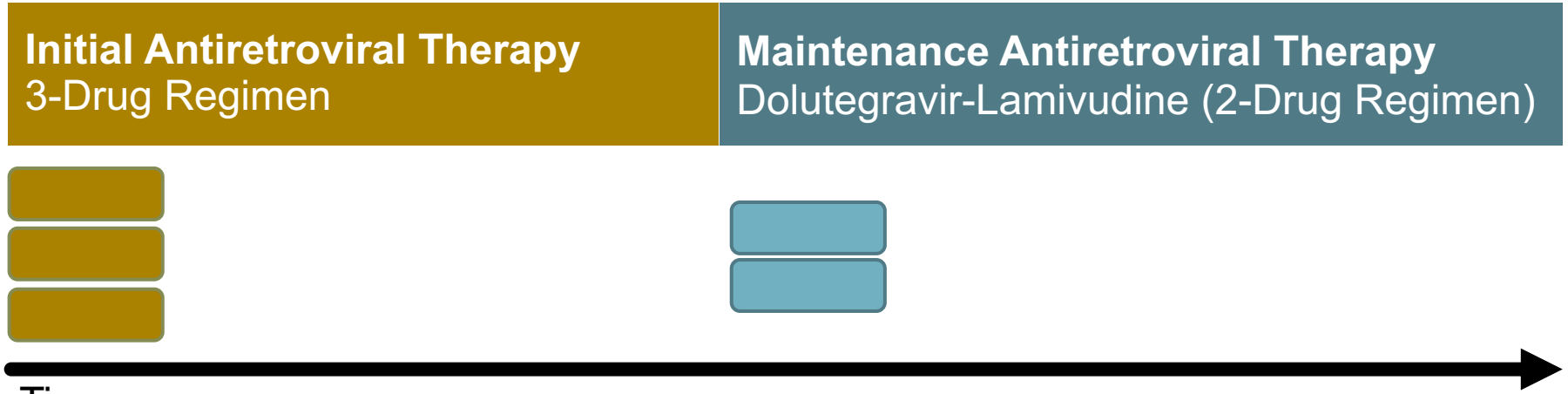


Baseline Requirements

- HIV RNA <500,000 copies/mL
- Hepatitis B surface antigen (HBsAg) negative
- Results from genotype known

HHS Antiretroviral Therapy Guidelines (September 21, 2022)

Dolutegravir-Lamivudine: **Maintenance Antiretroviral Therapy**



Requirements Prior to Switching

- HIV RNA <50 copies/mL for ≥6 months
- Hepatitis B surface antigen (HBsAg) negative
- No prior virologic failure
- No resistance to either maintenance drug

Dolutegravir-Lamivudine
Summary of Key Phase 3 Studies

- **Trials in in Treatment-Naïve Adults**
  - GEMINI-1: DTG-3TC versus DTG + TDF-FTC as Initial Therapy
  - GEMINI-2: DTG-3TC versus DTG + TDF-FTC as Initial Therapy

- **Switch Trials in Adults with Virologic Suppression**
  - ASPIRE: Switch to DTG plus 3TC vs. 3-Drug Maintenance Regimen
  - TANGO: Switch to DTG-3TC vs. 3- or 4-Drug Maintenance Regimen
  - SALSA: Switch to DTG-3TC vs. 3- or 4-Drug Maintenance Regimen

Abbreviations: DTG-3TC = dolutegravir-lamivudine; DTG = dolutegravir; TDF-FTC = tenofovir DF-emtricitabine

Dolutegravir-Lamivudine

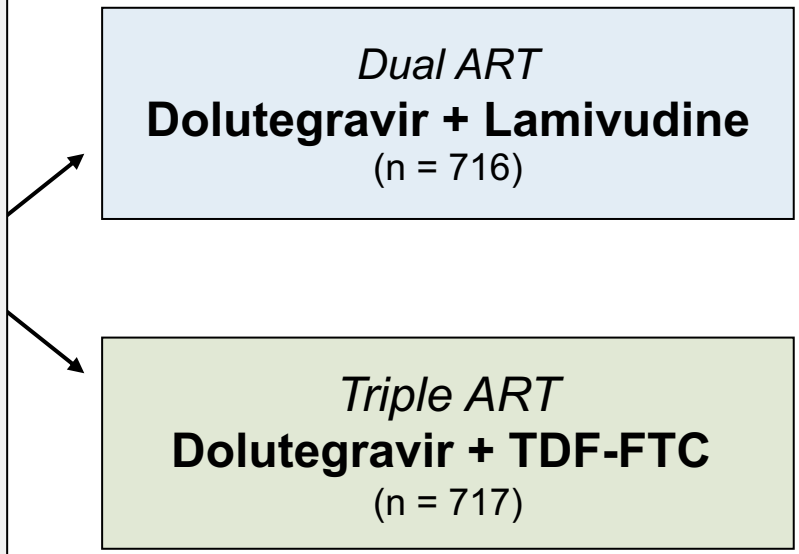
Trials in Treatment Treatment-Naïve Adults

DTG + 3TC versus DTG + TDF-FTC as Initial ART

GEMINI 1 and GEMINI 2: Week 48 Data

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and GEMINI 2: Background

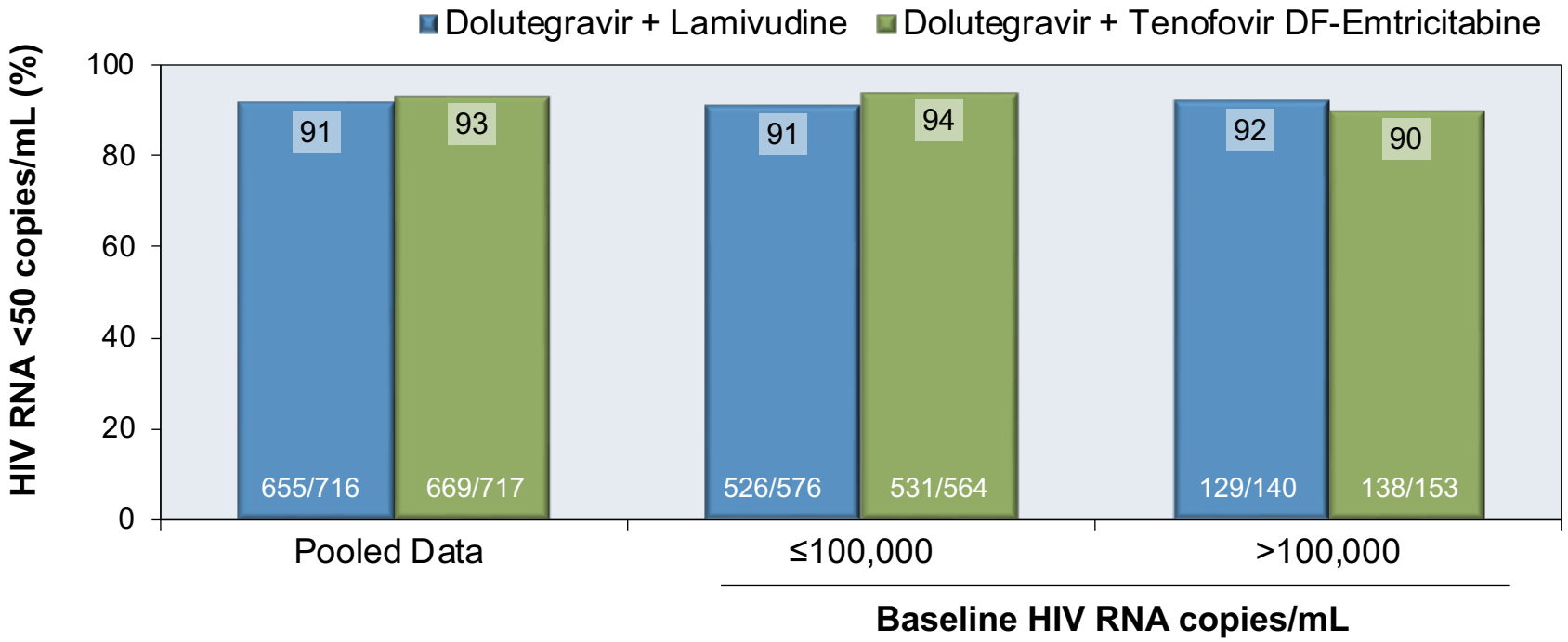
- **Background**
  - Two double-blind, multinational, noninferiority, randomized, controlled trials that compared initial ART of dolutegravir plus lamivudine (DTG + 3TC) versus dolutegravir plus tenofovir-DF-emtricitabine (DTG + TDF-FTC)
- **Enrollment Criteria**
  - Treatment-naïve adults
  - HIV RNA 1,000-500,000 copies/mL
  - No NRTI, INSTI, or major PI mutations
  - No chronic HBV
  - Not pregnant or breastfeeding



Source: Cahn P, et al. Lancet. 2019;393:143-55.

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and GEMINI 2: Results by Baseline HIV RNA Level

Week 48 Virologic Response (Intention-to-Treat Analysis)



Source: Cahn P, et al. Lancet. 2019;393:143-55.

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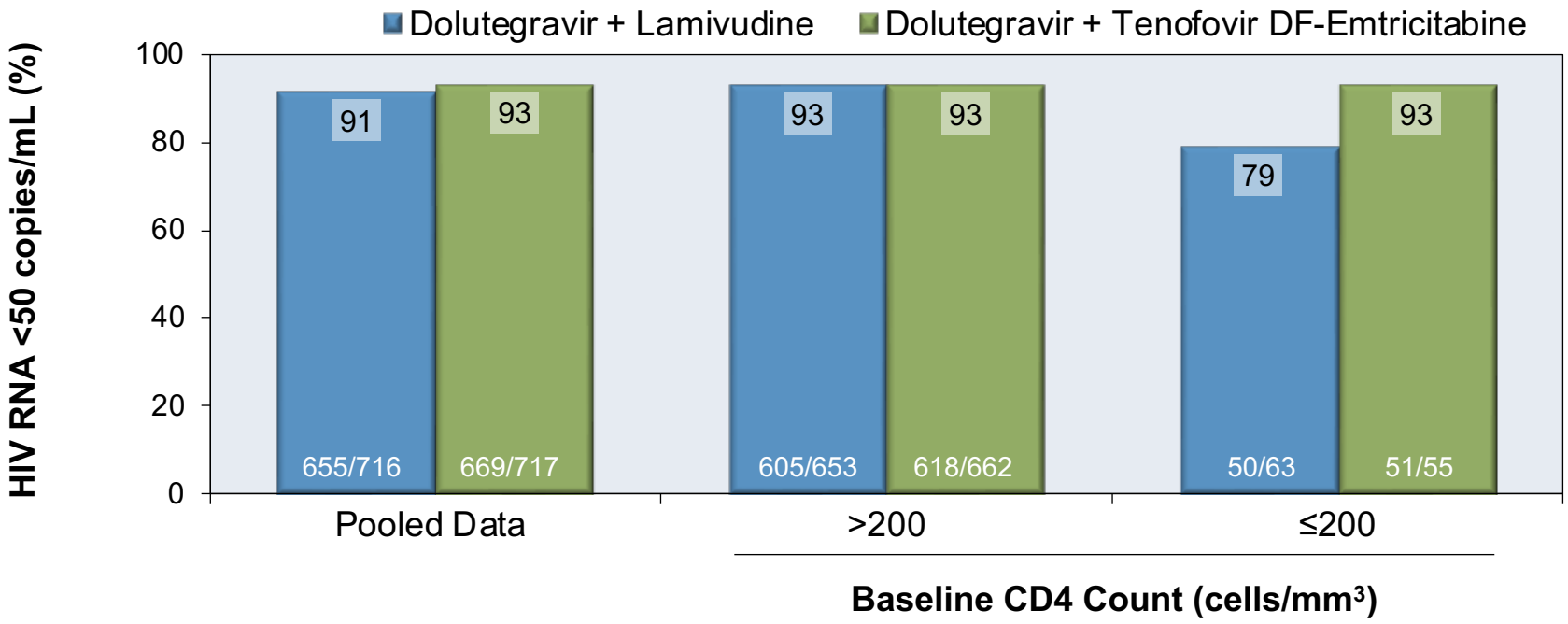
DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and GEMINI 2: Results by Baseline HIV CD4 Cell Count

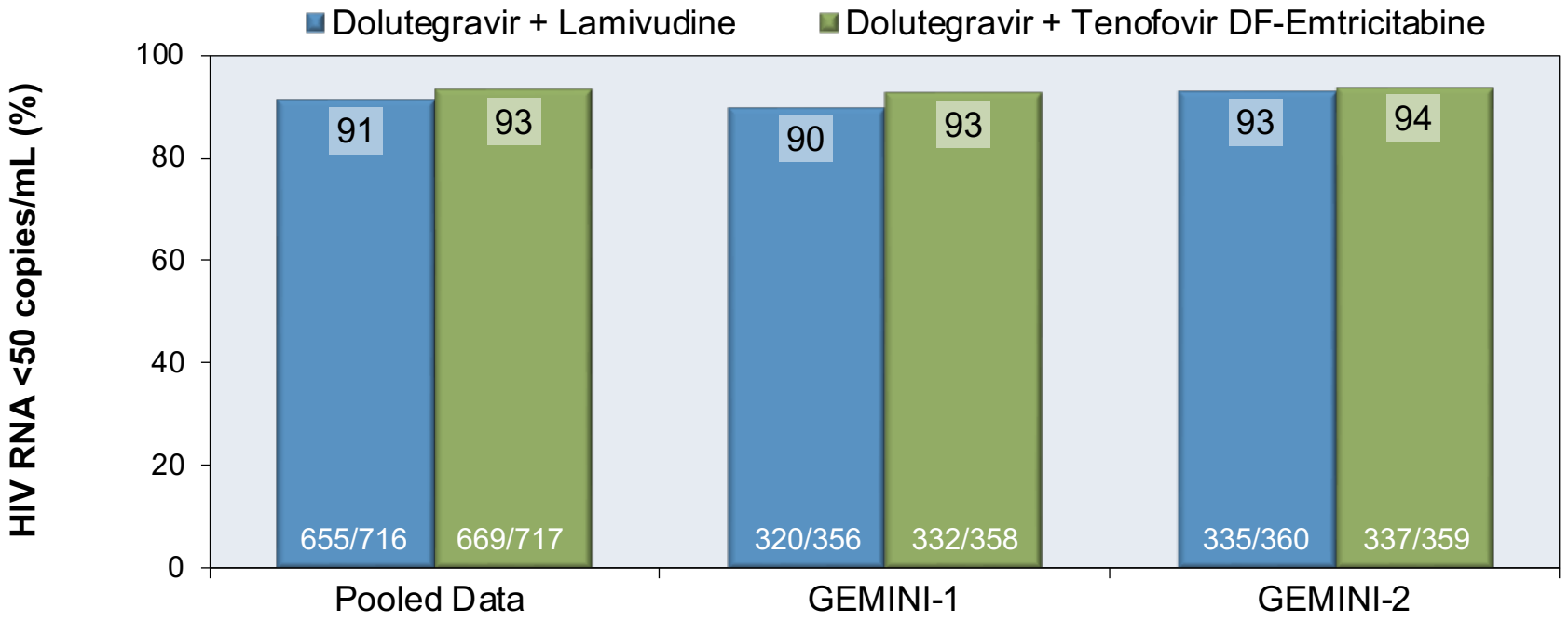
Week 48 Virologic Response (Intention-to-Treat Analysis)



Source: Cahn P, et al. Lancet. 2019;393:143-55.

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Results

Week 48 Virologic Response (Intention-to-Treat Analysis)



Source: Cahn P, et al. Lancet. 2019;393:143-55

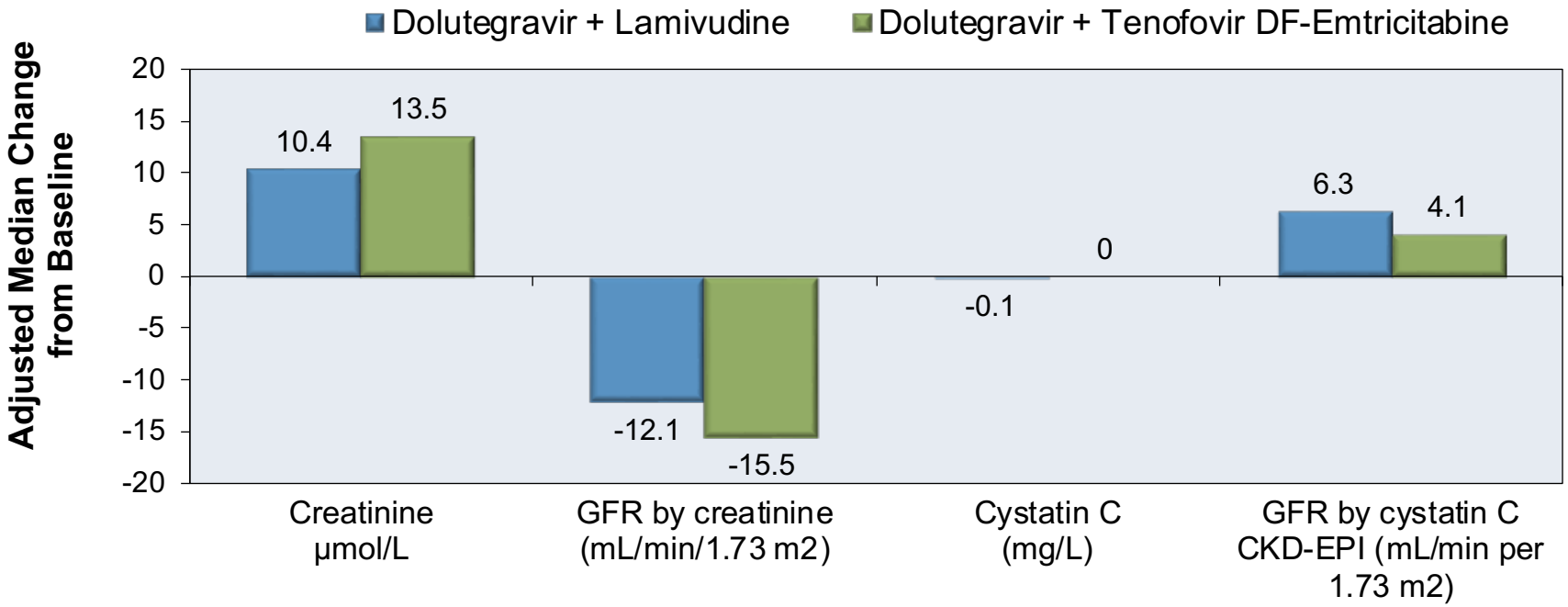
DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Baseline Characteristics

GEMINI 1 and 2 Baseline Characteristics		
Characteristic	**DTG + 3TC** (n = 716)	**DTG + TDF-FTC** (n = 717)
Age, years, median (IQR)	32 (26-40)	33 (26-42)
Female, n (%)	113 (16)	98 (14)
White, n (%)	480 (67)	497 (69)
Black or African American, n (%)	99 (14)	76 (11)
CD4 cell count, mean (SD)	462 (219.2)	461.3 (213.1)
CD4 count ≤200 cells/mm^3, n (%)	63 (9)	55 (8)
HIV RNA (log_{10} copies/mL)	4.42 (0.66)	4.45 (0.65)
≤100,000 copies/mL, n (%)	576 (80)	564(79)
>100,000 copies/mL, n (%)	140 (20)	153 (21)

Source: Cahn P, et al. Lancet. 2019;393:143-55.

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Results

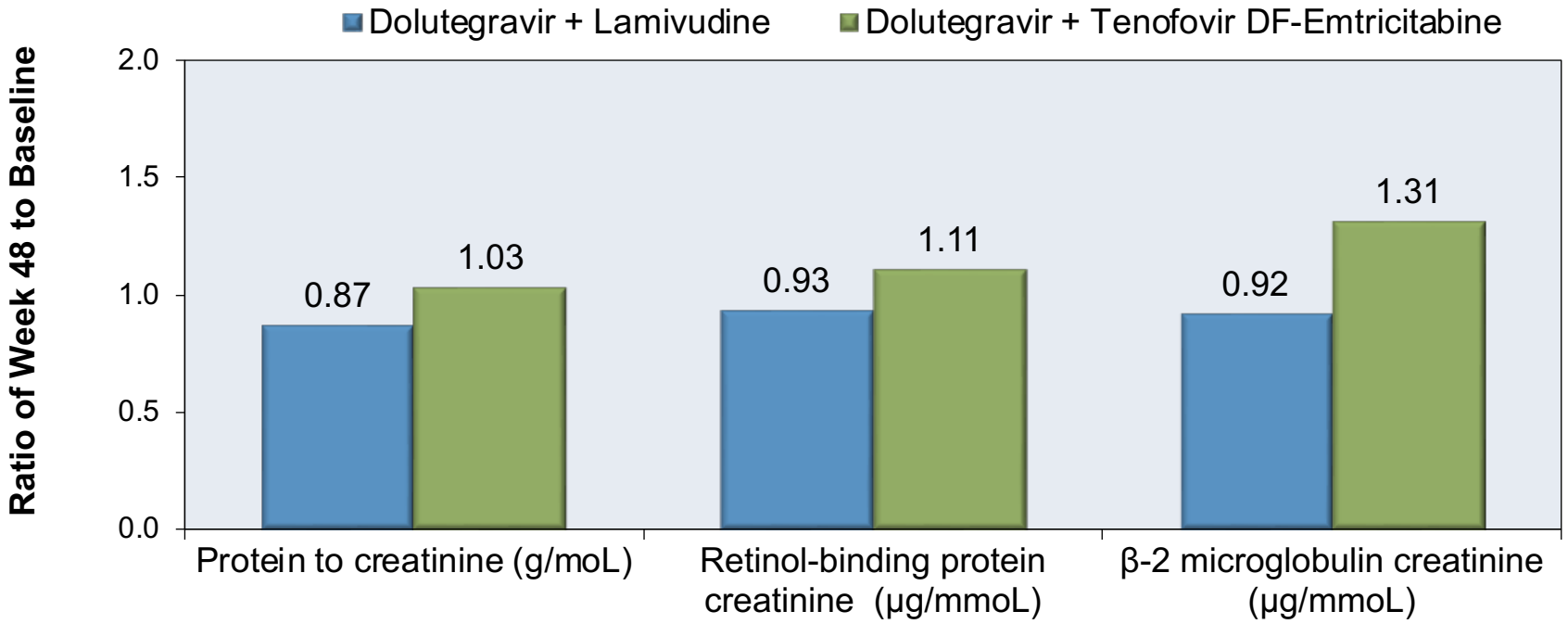
Week 48 Changes in Renal Function



Source: Cahn P, et al. Lancet. 2019;393:143-55.

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Results

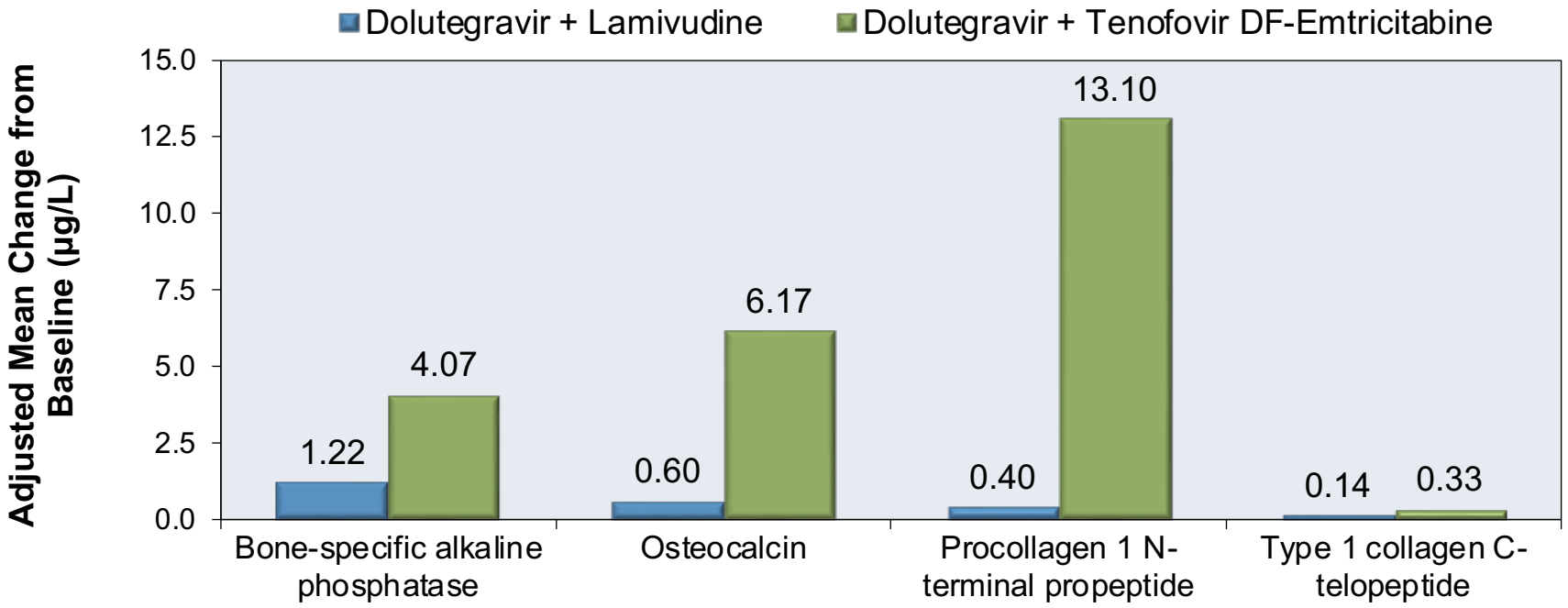
Week 48 Changes in Markers of Renal Proximal Tubulopathy



Source: Cahn P, et al. Lancet. 2019;393:143-55.

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Results

Week 48 Changes in Serum Bone Biomarkers



Source: Cahn P, et al. Lancet. 2019;393:143-55.

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Conclusions

Interpretation: “The non-inferior efficacy and similar tolerability profile of dolutegravir plus lamivudine to a guideline-recommended three-drug regimen at 48 weeks in ART-naive adults supports its use as initial therapy for patients with HIV-1 infection.”

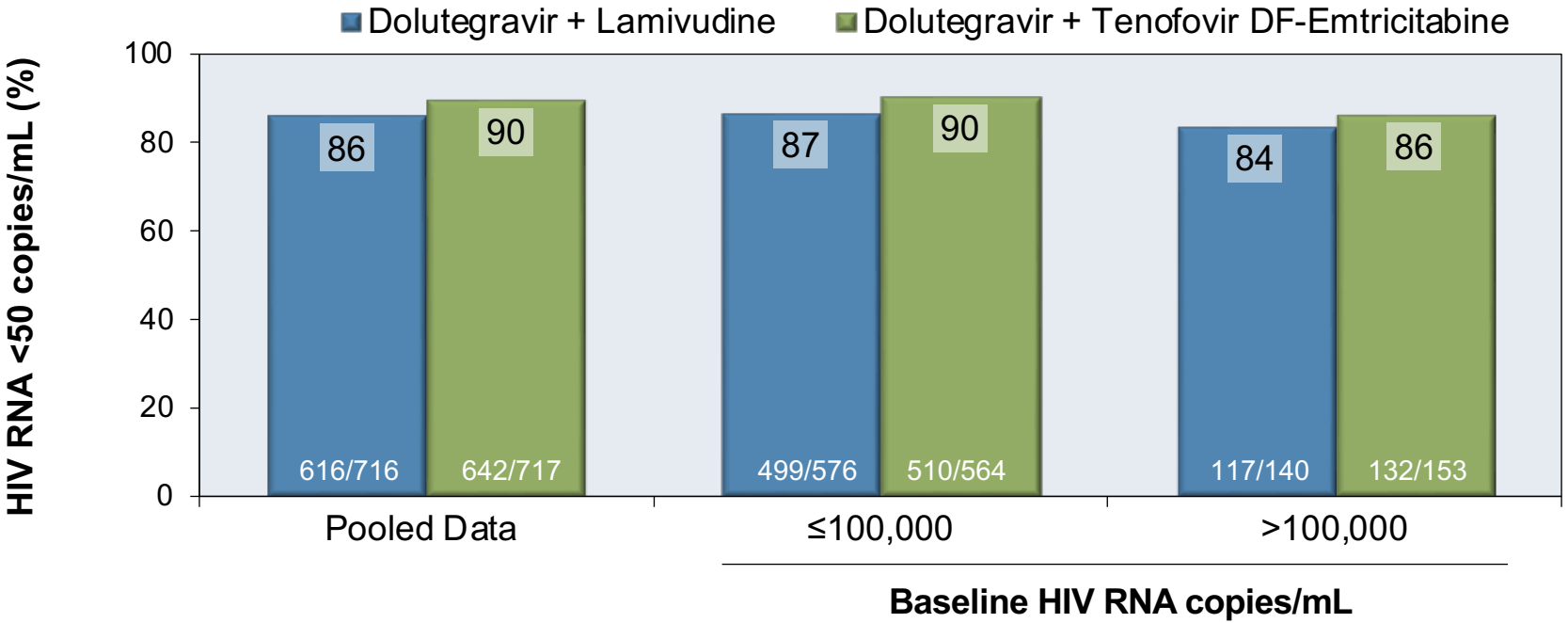
Source: Cahn P, et al. Lancet. 2019;393:143-55.

DTG + 3TC versus DTG + TDF-FTC as Initial ART

GEMINI 1 and GEMINI 2: Week 96 Data

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Results by Baseline HIV RNA Level

Week 96 Virologic Response (Intention-to-Treat Analysis)



Source: Cahn P, et al. J Acquir Immune Defic Syndrome. 2020;83:310-18.

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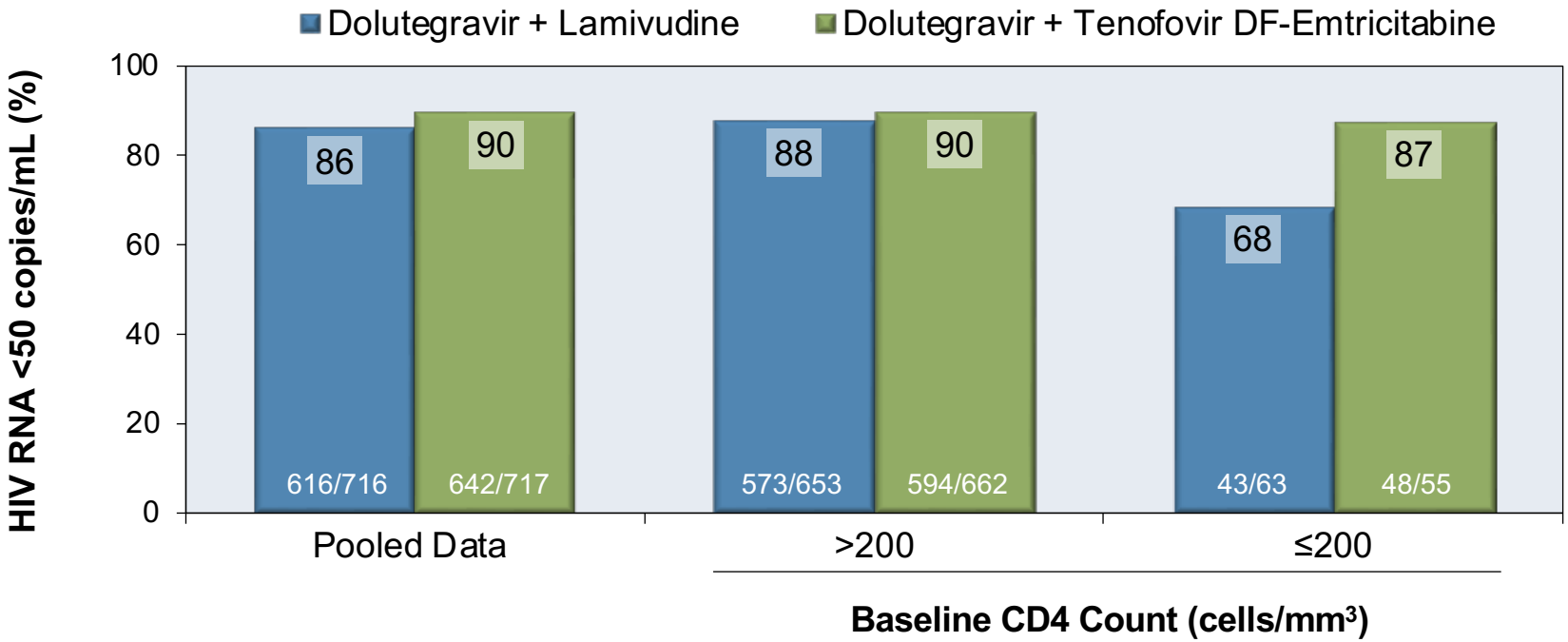
DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Results by Baseline CD4 Cell Count

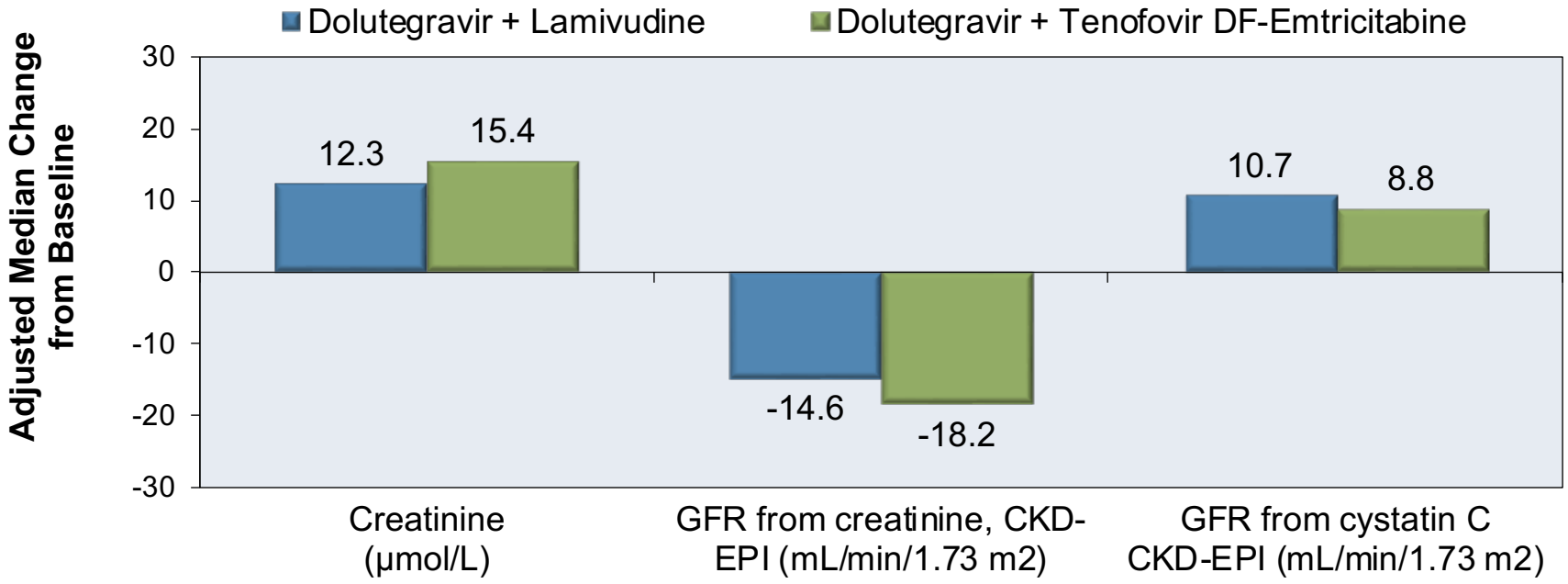
Week 96 Virologic Response (Intention-to-Treat Analysis)



Source: Cahn P, et al. J Acquir Immune Defic Syndrome. 2020;83:310-18.

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Results

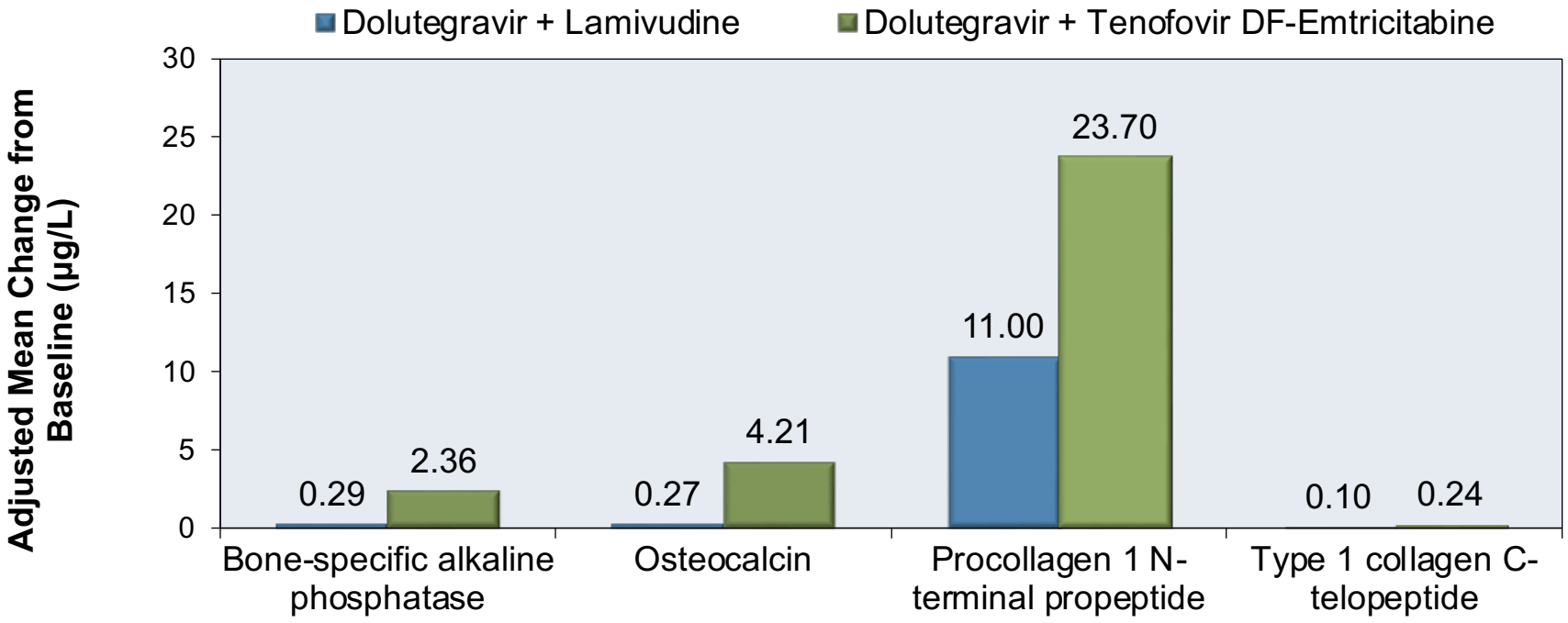
Week 96 Changes in Renal Function



Source: Cahn P, et al. J Acquir Immune Defic Syndrome. 2020;83:310-18.

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Results

Week 96 Changes in Serum Bone Biomarkers



Source: Cahn P, et al. J Acquir Immune Defic Syndrome. 2020;83:310-18.

DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Week 96 Conclusion

Conclusion: “Consistent with 48-week data, dolutegravir + lamivudine demonstrated long-term, non-inferior efficacy vs dolutegravir + tenofovir disoproxil fumarate/emtricitabine without increased risk of treatment emergent resistance, supporting its use in treatment-naive HIV-1–infected individuals.”

Source: Cahn P, et al. J Acquir Immune Defic Syndrome. 2020;83:310-18.

Dolutegravir-Lamivudine

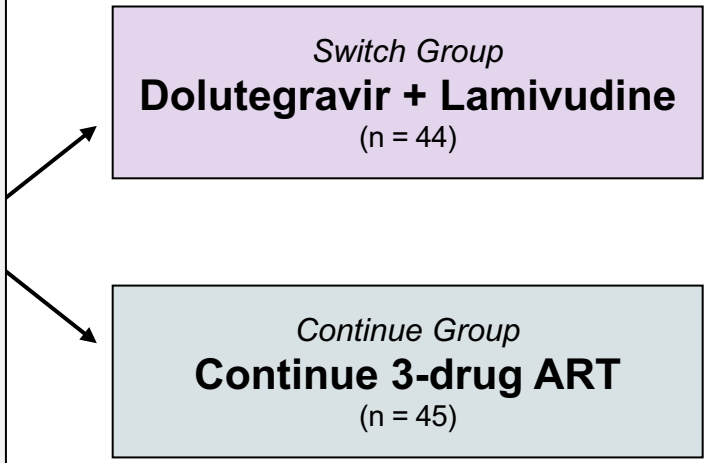
Switch Studies in Adults with Virologic Suppression

Switch to DTG + 3TC versus Continued 3-Drug ART

ASPIRE

Switch to DTG + 3TC versus Continued 3-Drug Antiretroviral Therapy
ASPIRE: Background

- **Background**: Open-label, multicenter, pilot randomized trial that enrolled persons with suppressed HIV RNA levels and compared switch to 2-drug regimen versus continuing standard 3-drug antiretroviral therapy
- **Inclusion Criteria:**
  - Adults (age >18 years) with HIV
  - HIV RNA <50 copies/mL at least twice over 48 weeks
  - Screening HIV RNA <20 copies/mL
  - Taking any 3-drug ART regimen
  - No history of virologic failure
  - No known NRTI or INSTI resistance mutations
  - No chronic HBV
  - CrCl ≥50 mL/min



Source: Taiwo B, et al. Clin Infect Dis. 2018;66:1794-7.

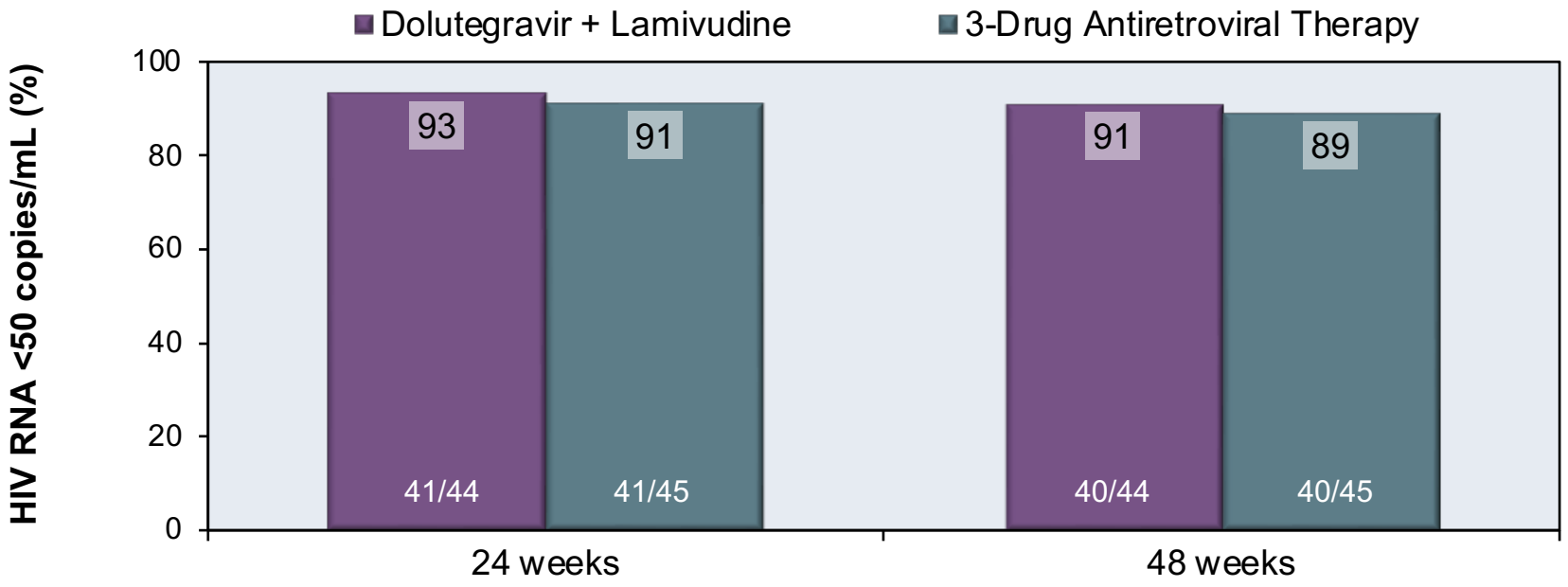
Switch to DTG + 3TC versus Continued 3-Drug Antiretroviral Therapy
ASPIRE: Baseline Characteristics

ASPIRE: Baseline Characteristics	
Characteristic	**Combined Group Study Population (n = 89)**
Age, years, median (IQR)	47 (38-54)
Male, %	88
White, %	60
Black or African American, %	38
Hispanic ethnicity, %	15
CD4 count, cells/mm^3, median (IQR)	680 (498-927)
Time on ART, years, median (IQR)	5.7 (3.7-7.5)
Pre-randomization INSTI, %	37
Pre-randomization PI, %	33
Pre-randomization NNRTI, %	30

Source: Taiwo B, et al. Clin Infect Dis. 2018;66:1794-7.

Switch to DTG + 3TC versus Continued 3-Drug Antiretroviral Therapy ASPIRE: Results at 24 & 48 Weeks

Week 24 & 48 Virologic Responses (Intention-to-Treat Analysis)



One virologic failure occurred in the dolutegravir + lamivudine arm; no resistance mutations detected

Source: Taiwo B, et al. Clin Infect Dis. 2018;66:1794-7.

Switch to DTG + 3TC versus Continued 3-Drug Antiretroviral Therapy ASPIRE: Conclusion

Conclusion: “In this randomized pilot clinical trial, dolutegravir plus lamivudine was noninferior to continuation of standard 3-drug maintenance antiretroviral therapy. There was no emergence of drug resistance in the participant who experienced virologic failure while receiving dolutegravir plus lamivudine.”

Source: Taiwo B, et al. Clin Infect Dis. 2018;66:1794-7.

Switch to Dolutegravir-Lamivudine versus Continued TAF-Based 3-Drug ART

TANGO

Switch to DTG-3TC versus Continued TAF-Based Baseline Regimen TANGO: Design

- **Design:** Open-label, non-inferiority trial in adults with suppressed HIV RNA while taking a 3- or 4-drug tenofovir alafenamide (TAF)-based regimen, randomized to switch to fixed-dose dolutegravir-lamivudine (DTG-3TC) or continue the baseline regimen
- **Inclusion Criteria**
  - Adults with suppressed HIV RNA >6 months
  - Taking 3- or 4-drug TAF-based ART
  - No history of virologic failure
  - No major NRTI resistance; no INSTI resistance
  - No hepatitis B or C
- **Regimens**
  - Dolutegravir-lamivudine (50/300mg) daily
  - TAF-based 3- or 4-drug baseline regimen

Switch Group

Dolutegravir-Lamivudine

(n = 369)

Continue Baseline Regimen Group

TAF-Based 3- or 4-Drug Regimen

(n = 372)

Source: van Wyk J, et al. Clin Infect Dis. 2020;71:1920-9.

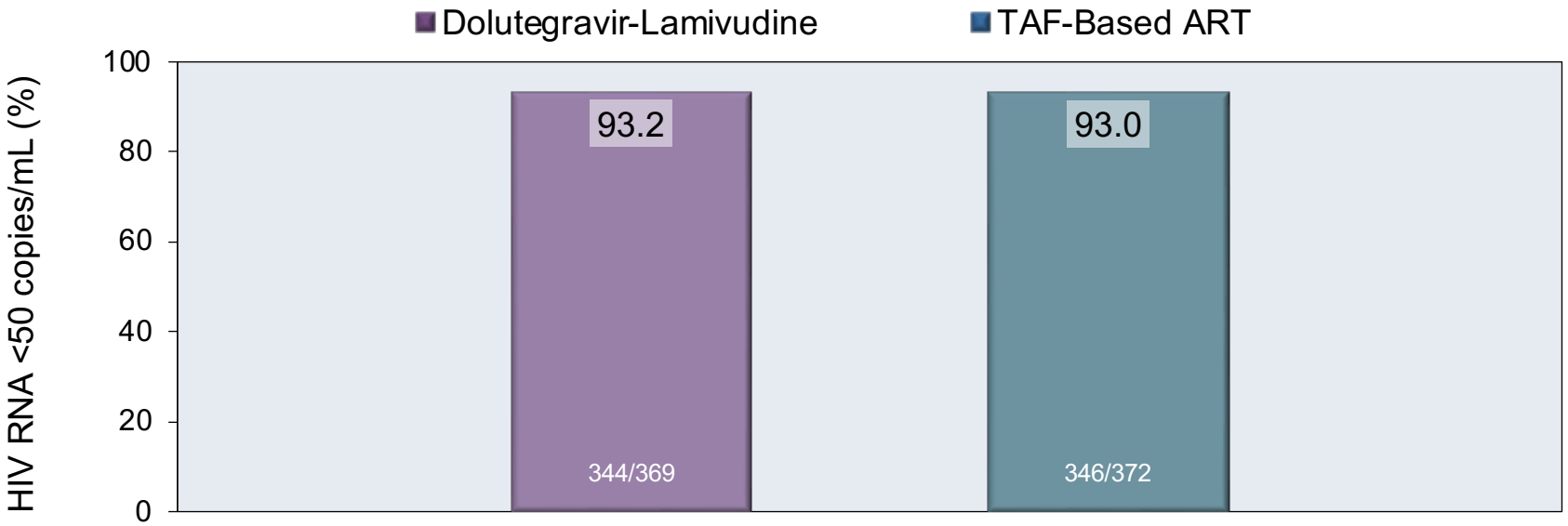
Switch to DTG-3TC versus Continued TAF-Based Baseline Regimen TANGO: Baseline Characteristics

Characteristic	Dolutegravir-Lamivudine (n = 369)	TAF-Based ART (n = 372)
Age, years, median (range)	40 (20-74)	39 (18-73)
Female, n (%)	25 (7)	33 (9)
White, n (%)	297 (81)	289 (78)
African American/African, n (%)	50 (14)	58 (16)
CD4 cell count <500, n (%)	98 (27)	74 (20)
CD4 cell count ≥500, n (%)	271 (73)	298 (80)
Months on ART, median (range)	33.8 (7.1-201.2)	35.1 (7.0-160.8)
Baseline third agent class		
INSTI	289 (78)	296 (80)
NNRTI	51 (14)	48 (13)
PI	29 (8)	28 (8)

Source: van Wyk J, et al. Clin Infect Dis. 2020;71:1920-9.

Switch to DTG-3TC versus Continued TAF-Based Baseline Regimen TANGO: Results at Week 48

Week 48 Virologic Response (Intention-to-Treat Snapshot Analysis)

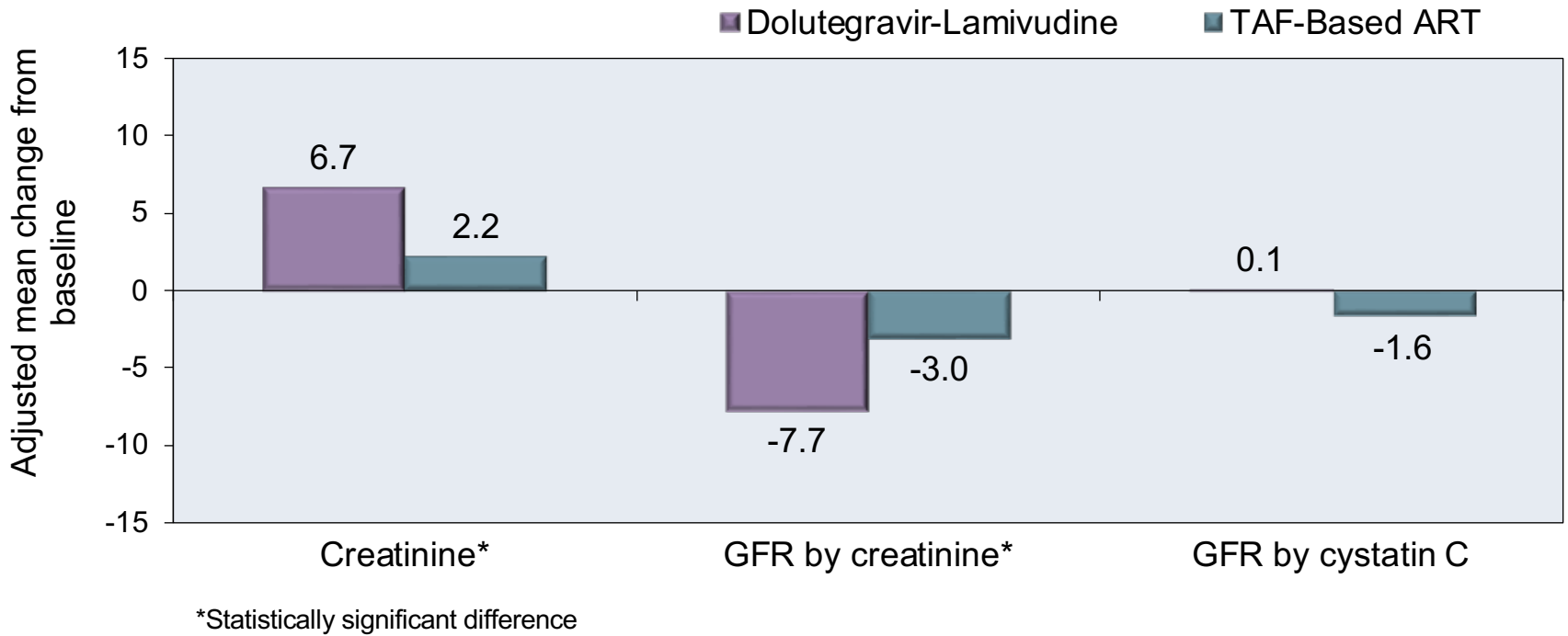


- Confirmed withdrawal for virologic failure: 0 in DTG/3TC arm, 1 in TAF-based ART arm
- No new resistance mutations occurred
- 4 with baseline M184V/I in DTG/3TC arm (by proviral genotype) suppressed at week 48

Source: van Wyk J, et al. Clin Infect Dis. 2020;71:1920-9.

Switch to DTG-3TC versus Continued TAF-Based Baseline Regimen TANGO: Results at Week 48

Week 48 Changes in Renal Function (Plasma/Serum Markers)

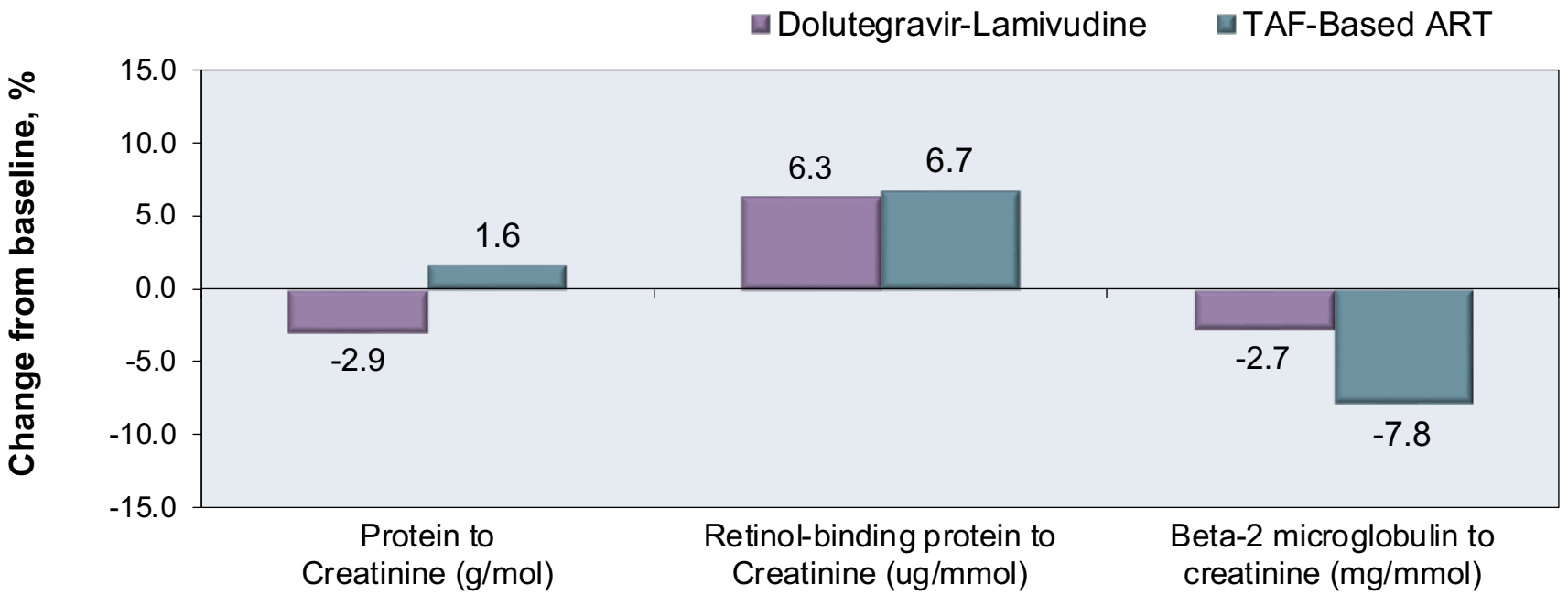


*Statistically significant difference

Source: van Wyk J, et al. Clin Infect Dis. 2020;71:1920-9.

Switch to DTG/3TC vs Continued TAF-Based 3-Drug ART
TANGO: Results at Week 48

Week 48 Changes in Markers of Proximal Tubulopathy (Urine Tests)



Source: van Wyk J, et al. Clin Infect Dis. 2020;71:1920-9.

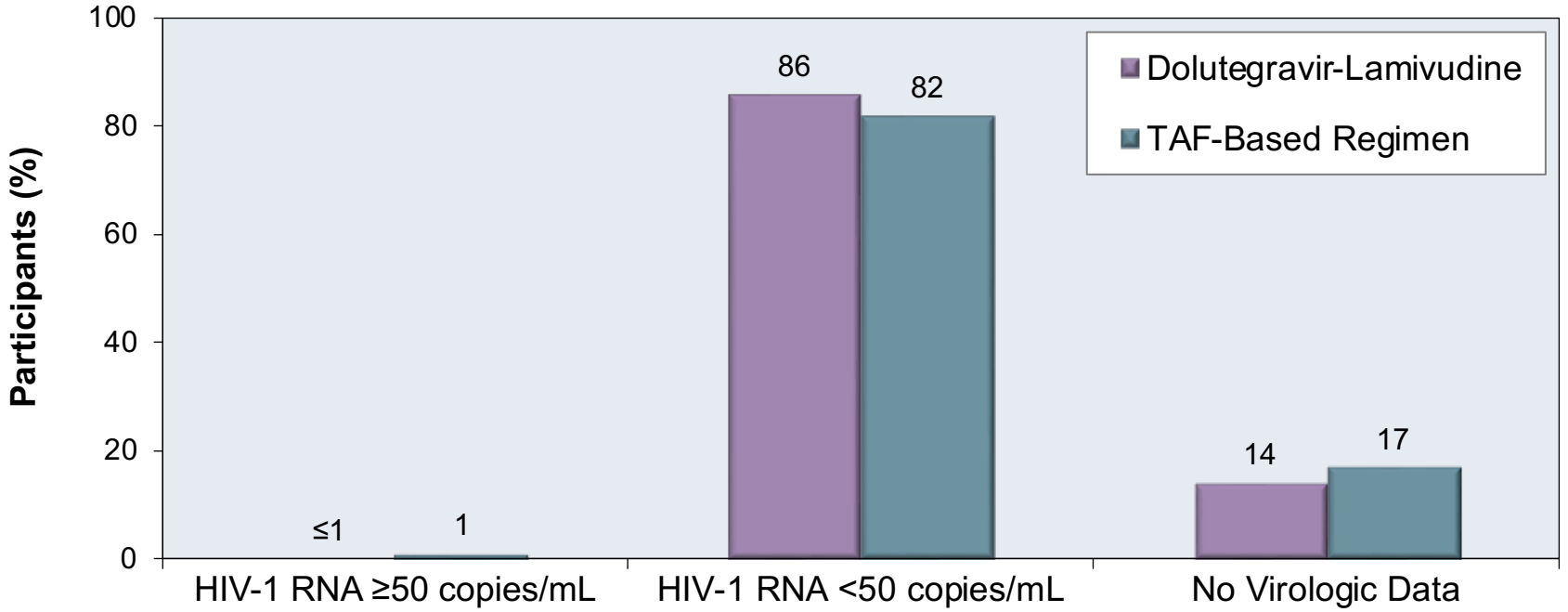
Switch to DTG-3TC versus Continued TAF-Based Baseline Regimen TANGO: Conclusions

Conclusion: “Dolutegravir-lamivudine was was noninferior in maintaining virologic suppression vs a TAF-based regimen at week 48, with no virologic failure or emergent resistance reported with DTG/3TC, supporting it as a simplification strategy for virologically suppressed people with HIV-1.”

Source: van Wyk J, et al. Clin Infect Dis. 2020;71:1920-9.

Switch to DTG-3TC versus Continued TAF-Based Baseline Regimen TANGO: 144 Week Results

Week 144 Virologic Response (ITT-Exposed)



Source: Osiyemi O, et al. Clin Infect Dis. 2022;75:975-86.

Switch to DTG-3TC versus Continued TAF-Based Baseline Regimen TANGO: Conclusions

Conclusion: “The 2-drug regimen dolutegravir-lamivudine was non-inferior in maintaining virologic suppression vs a tenofovir alafenamide-based regimen at Week 48, with no virologic failure or emergent resistance reported in the dolutegravir-lamivudine group, supporting its use as a simplification strategy for virologically suppressed people living with HIV-1.”

Source: Osiyemi O, et al. Clin Infect Dis. 2022;75:975-86.

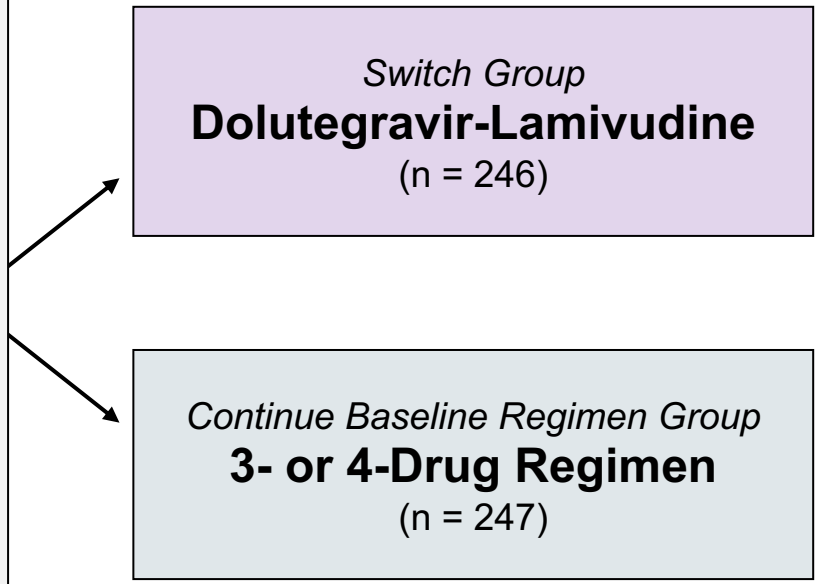
Switch to DTG-3TC versus Continued 3- or 4-Drug ART

SALSA

National HIV Curriculum

Switch to DTG-3TC versus Continued 3- or 4-Drug Regimen
SALSA: Design

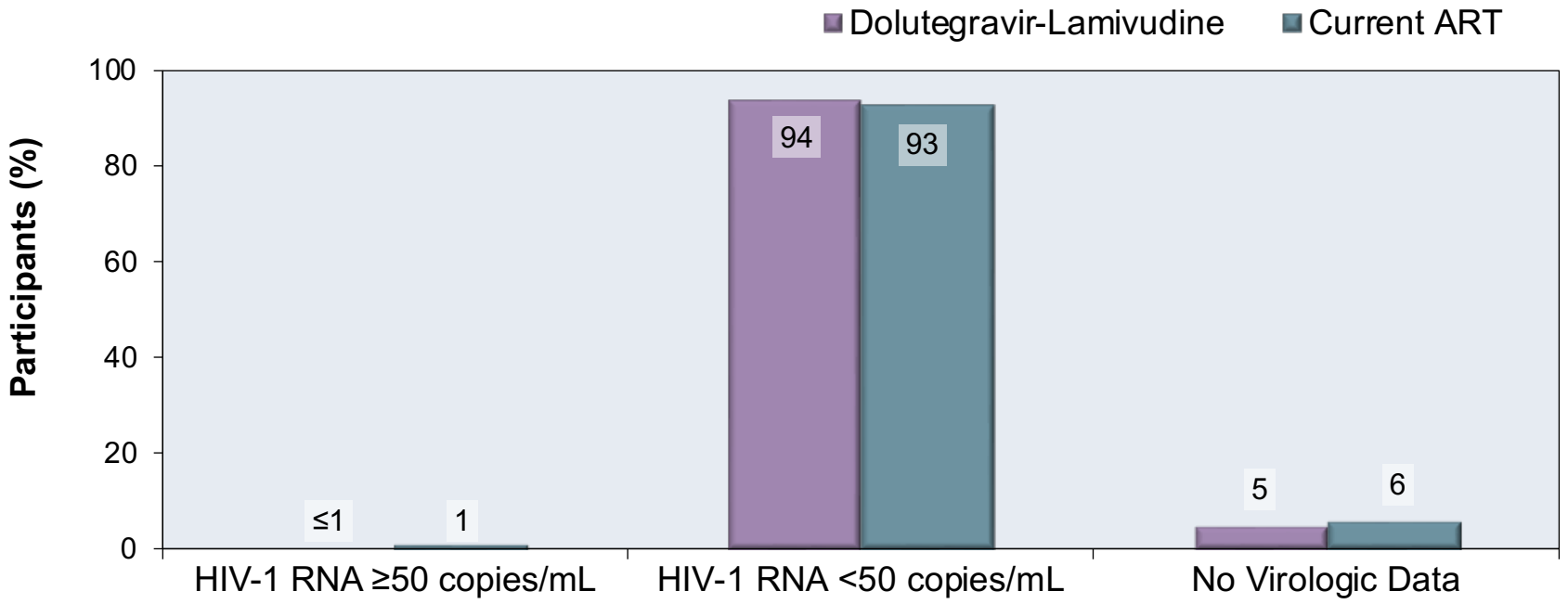
- **Design:** Open-label, non-inferiority trial in adults with suppressed HIV RNA while taking a 3- or 4-drug regimen, randomized to switch to fixed-dose dolutegravir-lamivudine (DTG-3TC) or continue baseline regimen
- **Inclusion Criteria**
  - Adults with suppressed HIV RNA ≥6 months
  - No history of virologic failure
  - No major NRTI resistance; no INSTI resistance
  - No Hepatitis B or C
- **Regimens**
  - Dolutegravir-lamivudine (50/300mg) daily
  - 3- or 4-drug baseline regimen



Source: Llibre JM, et al. Clin Infect Dis. 2022; Mar 2. Online ahead of print.

Switch to DTG-3TC versus Continued 3- or 4-Drug Regimen
SALSA: 48 Week Results

Week 48 Virologic Response ITT-Exposed (Snapshot Analysis)



Source: Llibre JM, et al. Clin Infect Dis. 2022; Mar 2. Online ahead of print.

Switch to DTG-3TC versus Continued 3- or 4-Drug Regimen
SALSA: Conclusions

Conclusion: “Switching to dolutegravir-lamivudine was non-inferior to continuing current antiretroviral regimen for maintaining virologic suppression at Week 48 with no observed resistance, supporting the efficacy, good safety, and high barrier to resistance of dolutegravir-lamivudine.”

Source: Llibre JM, et al. Clin Infect Dis. 2022; Mar 2. Online ahead of print.

Acknowledgments

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AETC AIDS Education & Training Center Program

National HIV Curriculum

IDEA INFECTIOUS DISEASES EDUCATION & ASSESSMENT