National HIV Curriculum

Doravirine-Tenofovir DF-Lamivudine (*Delstrigo*)

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Doravirine-Tenofovir DF-Lamivudine Single-Tablet Regimen

Doravirine-Tenofovir DF-Lamivudine

100 mg	300 mg	300 mg
NNRTI	NRTI	NRTI

Dose: 1 tablet once daily with or without food

Source: Photograph of Delstrigo tablet courtesy of Merck

Doravirine-Tenofovir DF-Lamivudine (DOR-TDF-3TC)

- **Indications for Adults and Pediatric (weight ≥35 kg)**
  - Treatment-naïve
  - Replace regimen in virologically suppressed and no failure or resistance to DRV, TDF, or 3TC
- **Dosing**
  - 1 tablet daily with or without food
- **With Renal Impairment**
  - Not recommended if CrCl less than 50 mL/min
- **With Hepatic Impairment**
  - No dose adjustment for Child-Pugh A or B; insufficient data for Child-Pugh C
- **Pregnancy**
  - Inadequate data
- **Common Adverse Effects (≥5%)**
  - Dizziness, nausea, and abnormal dreams

Doravirine-Tenofovir DF-Lamivudine
Summary of Key Phase 3 Studies

- **Trials in in Treatment-Naïve Adults**
  - DRIVE AHEAD: DOR-TDF-3TC vs. EFV-TDF-FTC as Initial Therapy
- **Trials in Adults with Virologic Suppression**
  - DRIVE SHIFT: Switch to DOR-TDF-3TC vs. Maintenance Regimen

Abbreviations: DOR-TDF-FTC = doravirine-tenofovir DF-lamivudine; EFV-TDF-FTC = efavirenz-tenofovir DF-emtricitabine

Doravirine-Tenofovir DF-Lamivudine

Trials in Treatment Treatment-Naïve Adults

DOR-TDF-3TC vs. EFV-TDF-FTC as Initial Therapy

DRIVE AHEAD

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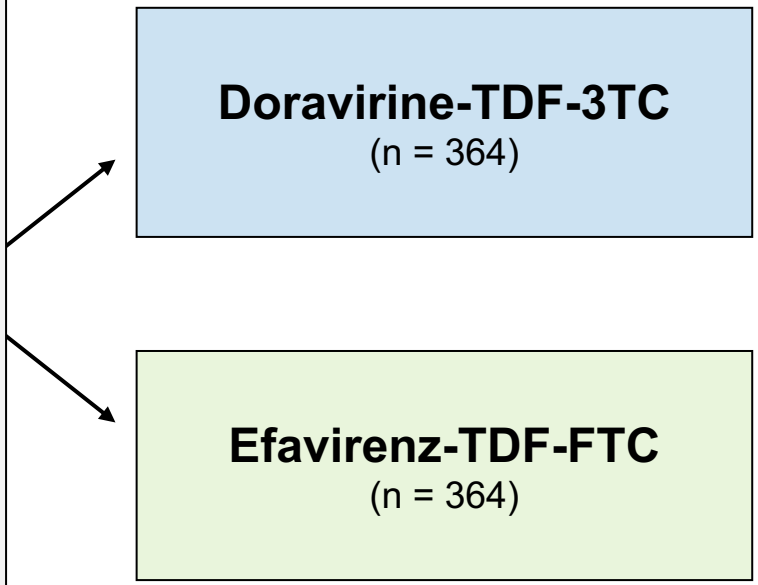
Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy
DRIVE AHEAD: Design

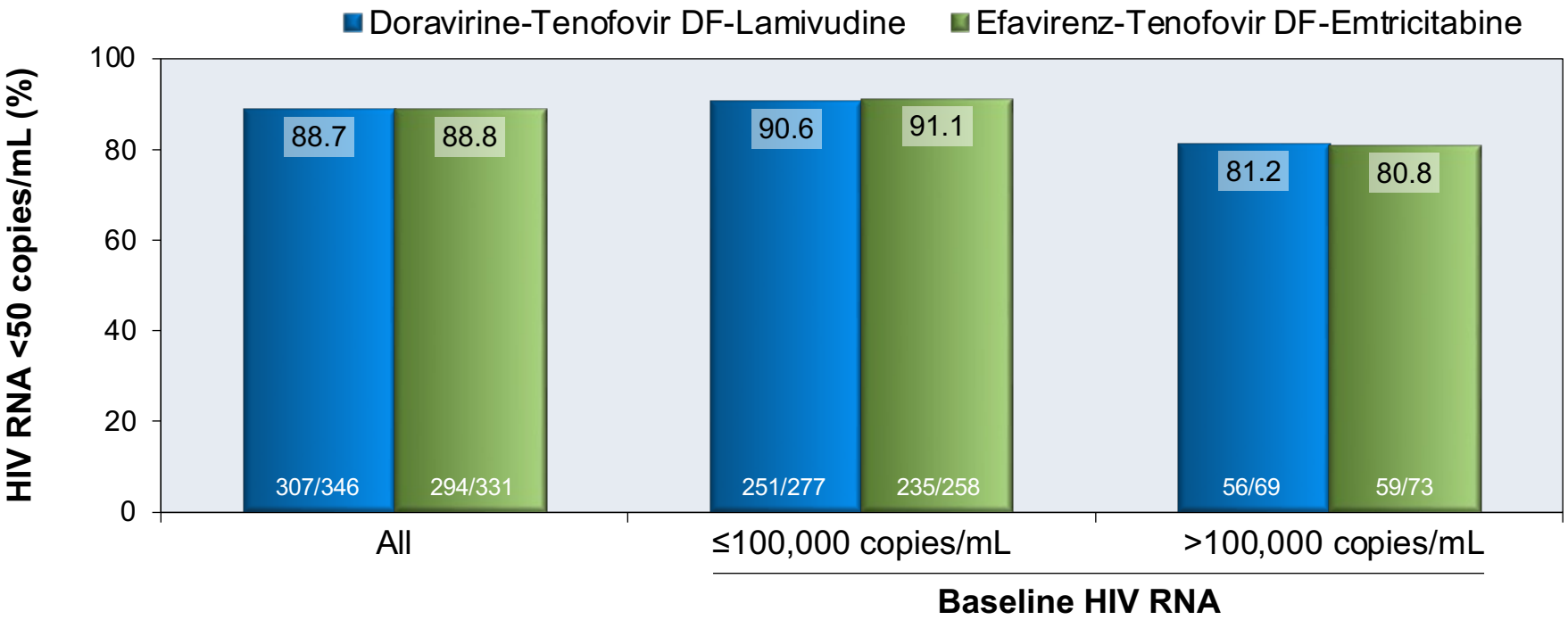
- **Design**
  - Randomized, double-blind, phase 3 study comparing fixed dose doravirine-tenofovir DF-lamivudine with fixed dose efavirenz-tenofovir DF-emtricitabine as initial antiretroviral therapy
- **Inclusion Criteria**
  - Antiretroviral-naïve
  - Age ≥18 years
  - HIV RNA ≥1,000 copies/mL
  - No resistance to any study drug
- **Regimens**
  - Doravirine-TDF-3TC (100/300/300 mg) daily
  - Efavirenz-TDF-FTC (600/300/200 mg) daily



Source: Orkin C, et al. Clin Infect Dis. 2019;68:535-44.

Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy
DRIVE AHEAD: 48 Week Results

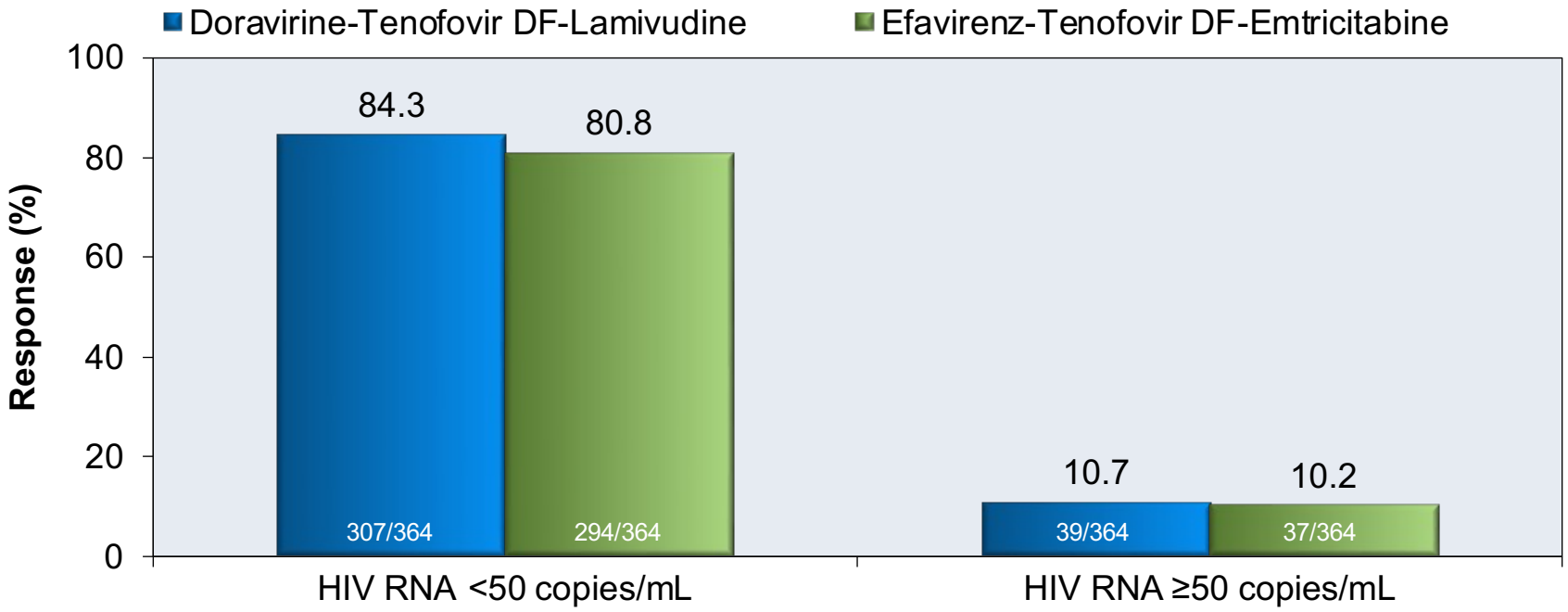
Week 48 Virologic Response (Observed Failure)



Source: Orkin C, et al. Clin Infect Dis. 2019;68:535-44.

Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy
DRIVE AHEAD: Results

Week 48 Virologic Response (FDA Snapshot: All missing data = Failure)



Source: Orkin C, et al. Clin Infect Dis. 2019:68:535-44.

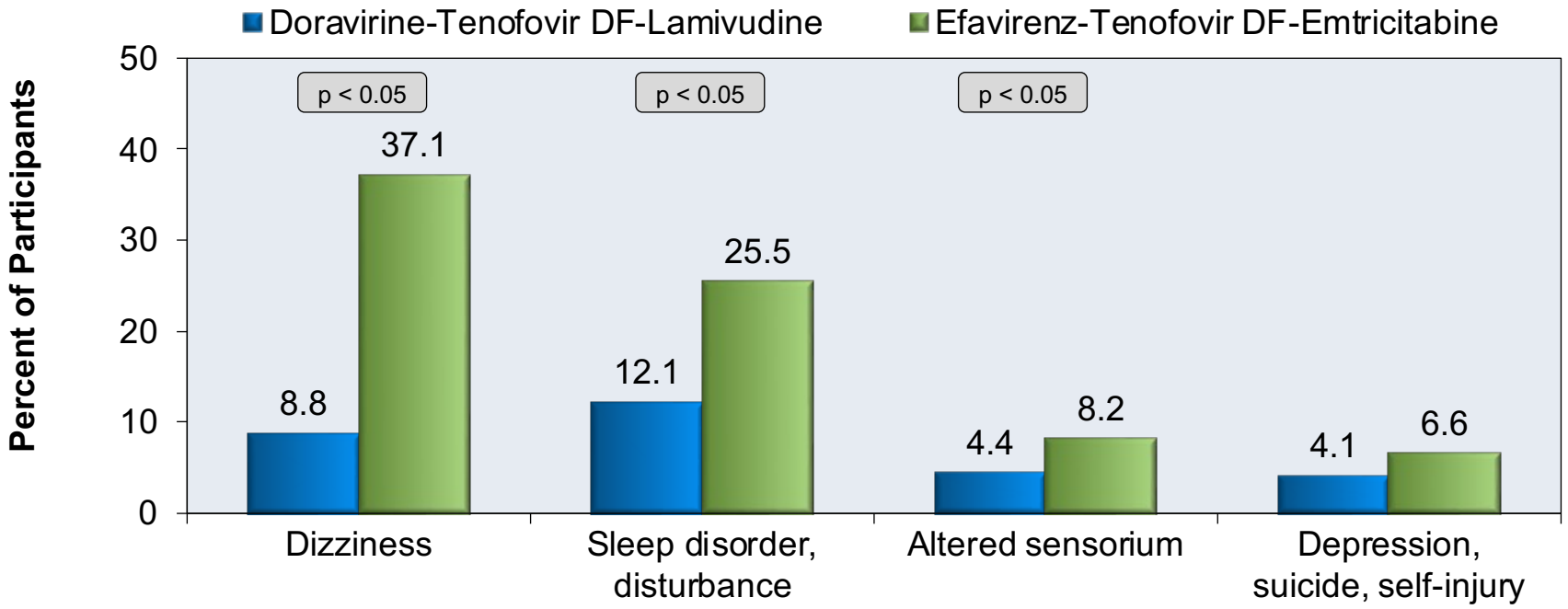
Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy
DRIVE AHEAD: Adverse Effects

Treatment Emergent Adverse Events in DRIVE AHEAD Through Week 48		
Adverse Effects	**DOR/TDF/3TC** (n = 364)	**EFV/TDF/FTC** (n = 364)
Drug-related AE's, %	31	63
Discontinued due to drug-related AE, %	3	7
Headache, %	13	12
Diarrhea, %	11	13
Nausea, %	8	11
Vomiting, %	4	7
Abnormal Dreams, %	5	12
Rash, %	5	12

Source: Orkin C, et al. Clin Infect Dis. 2019:68:535-44.

Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy
DRIVE AHEAD: Adverse Effects

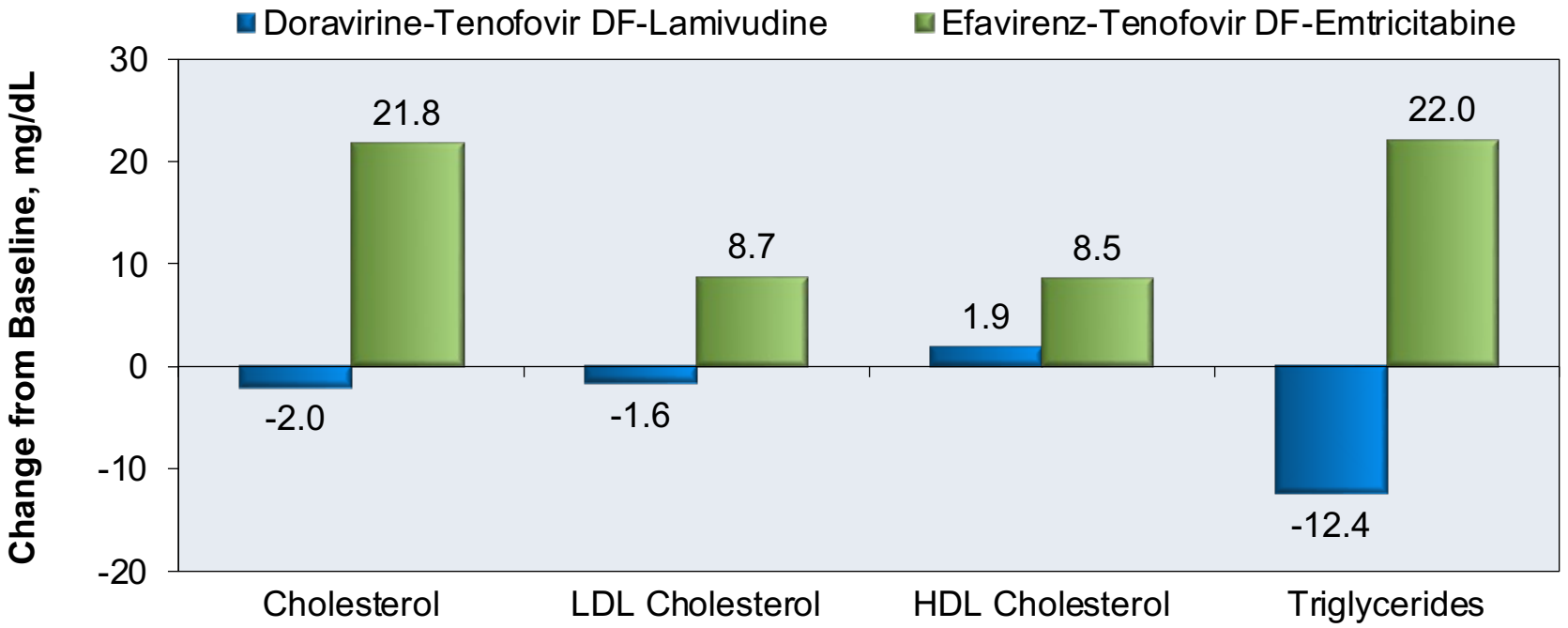
Proportion with Pre-Defined Neuropsychiatric Side Effects at Week 48



Source: Orkin C, et al. Clin Infect Dis. 2019:68:535-44.

Doravirine-TDF-3TC versus Efavirenz-TDF-FTC as Initial Therapy
DRIVE AHEAD: Adverse Effects

Change in Baseline Fasting Lipids at Week 48



Source: Orkin C, et al. Clin Infect Dis. 2019:68:535-44.

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DOR-TDF-3TC vs. EFV-TDF-FTC as Initial Therapy
DRIVE AHEAD: Summary

Conclusions: “In HIV-1 treatment-naive adults, doravirine/lamivudine/tenofovir DF demonstrated non-inferior efficacy to efavirenz/emtricitabine/tenofovir DF at week 48 and was well tolerated, with significantly fewer neuropsychiatric events and minimal changes in LDL-C and non-HDL-C compared with efavirenz/emtricitabine/tenofovir DF.”

Source: Orkin C, et al. Clin Infect Dis. 2019:68:535-44.

Doravirine-Tenofovir DF-Lamivudine

Switch Studies in Adults with Virologic Suppression

Switch to DOR-TDF-3TC vs. Continued Baseline Regimen

DRIVE SHIFT

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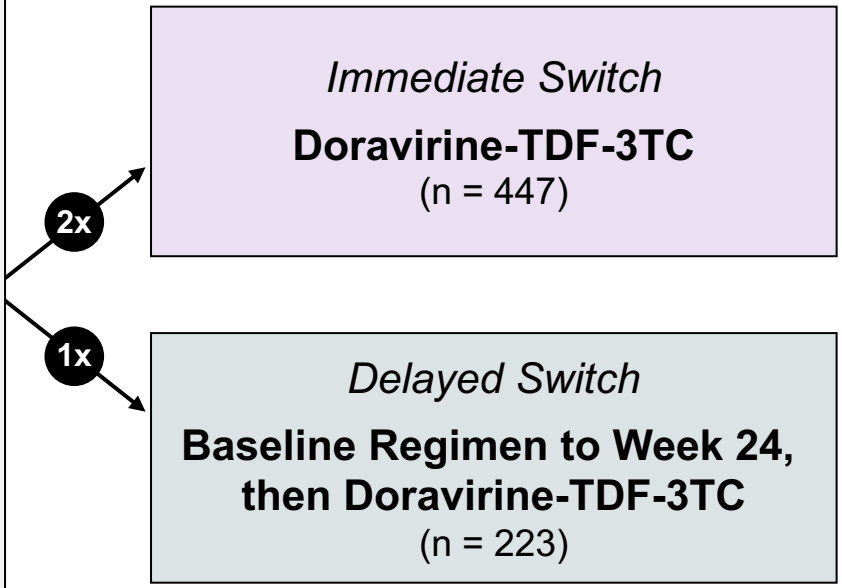
Switch to Doravirine-TDF-3TC versus Continued Baseline Regimen
DRIVE SHIFT: Design

- **Design:** Open-label, non-inferiority trial in adults with suppressed HIV RNA while taking 2 NRTIs plus anchor drug, randomized (2:1) to immediately switch to fixed-dose doravirine-tenofovir-DF-lamivudine or continue the baseline regimen with delayed switch at 24 weeks
- **Inclusion Criteria**
  - Age ≥18 years
  - Suppressed HIV RNA ≥6 months
  - No history of virologic failure
- **Baseline Regimen**
  - 2 NRTIs + (boosted protease inhibitor, boosted elvitegravir, or NNRTI)



Source: Johnson M, et al. J Acquir Immun Defic Syndr. 2019;81:463-72.

Switch to Doravirine-TDF-3TC versus Continued Baseline Regimen
DRIVE SHIFT: Baseline Characteristics

DRIVE SHIFT: Baseline Characteristics		
Characteristic	**Immediate Switch** (n = 447)	**Delayed Switch** (n = 223)
Age in years, median (range)	43 (21-71)	42 (22-71)
Male, n (%)	372 (83.2)	194 (87.0)
White, n (%)	344 (77.0)	168 (75.3)
Black or African American, n (%)	56 (12.5)	34 (15.2)
CD4 count (cells/mm^3), median (range),	633 (82-1,928)	625 (140-1,687)
CD4 count <200 cells/mm^3, n (%)	13 (2.9)	4 (1.8)
Median months on prior regimen (range)	48.4 (7-265)	50.5 (7-181)
Baseline mutations: K103N, Y181C, +/- G190A, n (%)	11 (2.5)	13 (5.8)
HBV and/or HCV coinfection, n (%)	14 (3.1)	9 (4.0)

Source: Johnson M, et al. J Acquir Immun Defic Syndr. 2019;81:463-72.

Switch to Doravirine-TDF-3TC versus Continued Baseline Regimen
DRIVE SHIFT: Baseline Antiretroviral Regimens

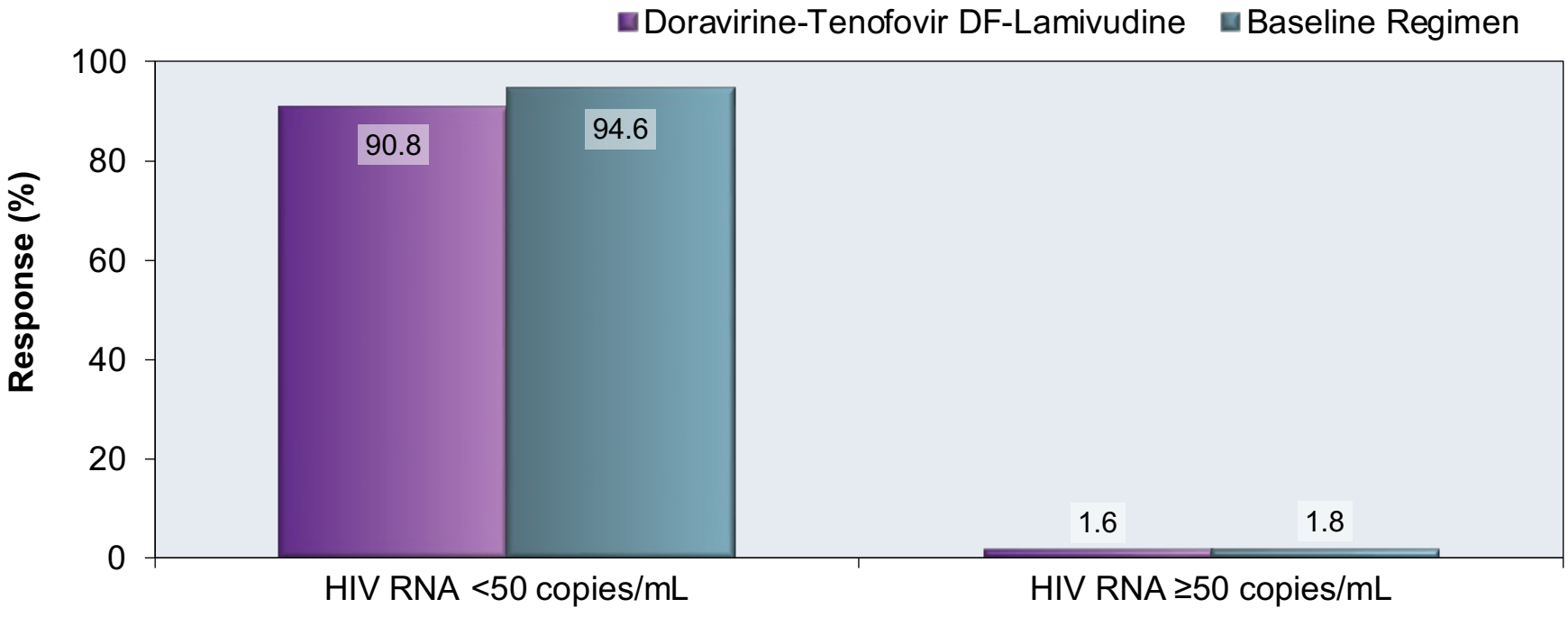
DRIVE SHIFT Baseline Antiretroviral Regimens		
Anchor Agent, n (%)	**Immediate Switch** (n = 447)	**Delayed Switch** (n = 223)
Boosted PI	316 (70.7)	156 (70.0)
Darunavir	166 (37.1)	82 (36.8)
Atazanavir	96 (21.5)	43 (19.3)
Lopinavir	54 (12.1)	31 (13.9)
Elvitegravir-cobicistat	25 (5.6)	12 (5.4)
NNRTI	106 (23.7)	55 (24.7)
Efavirenz	78 (17.4)	36 (16.1)
Nevirapine	17 (3.8)	12 (5.4)
Rilpivirine	11 (2.5)	7 (3.1)

*Most common NRTI backbone in both arms: TDF/FTC (73.8% in immediate switch, 69.1% in delayed switch)

Source: Johnson M, et al. J Acquir Immun Defic Syndr. 2019;81:463-72.

Switch to Doravirine-TDF-3TC versus Continued Baseline Regimen DRIVE SHIFT: Results

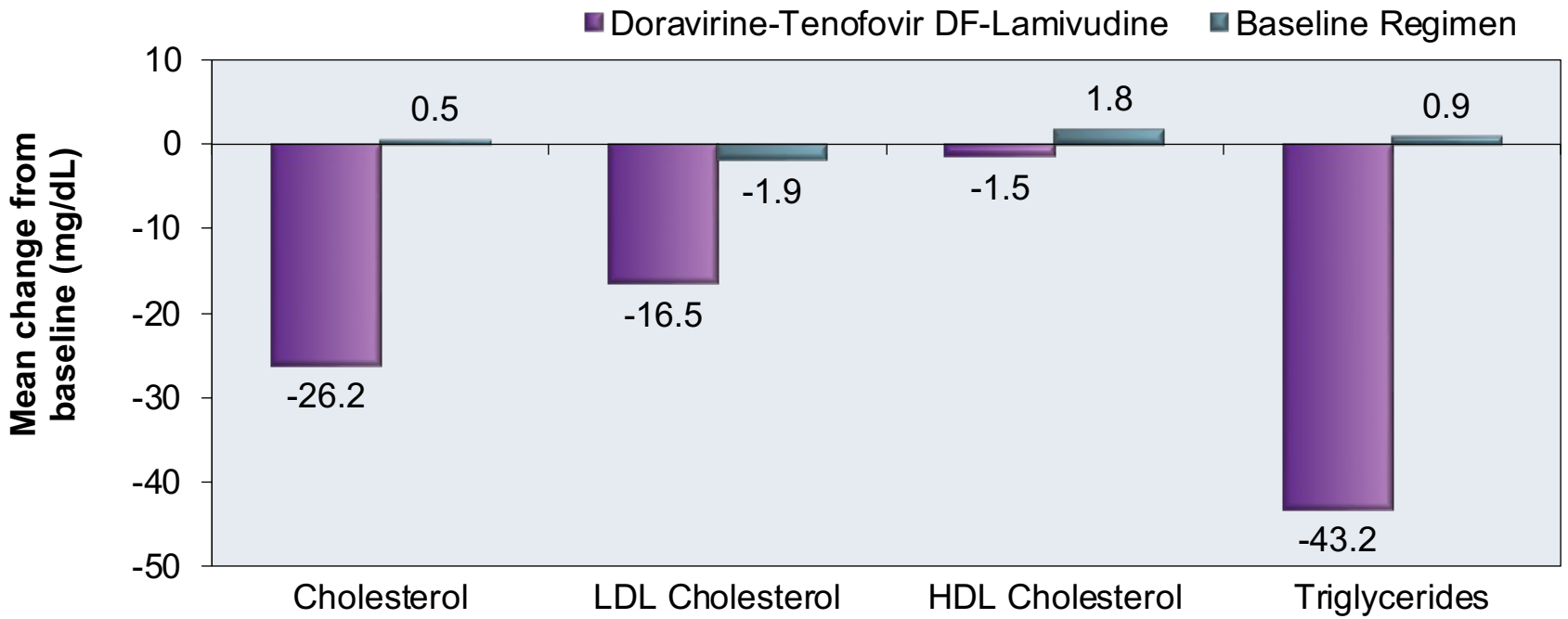
Week 48 Doravirine-TDF-3TC vs Week 24 Baseline Regimen (FDA snapshot)



Source: Johnson M, et al. J Acquir Immun Defic Syndr. 2019;81:463-72.

Switch to Doravirine-TDF-3TC versus Continued Baseline Regimen DRIVE SHIFT: Adverse Effects

Change in Fasting Lipids in Participants Taking a Boosted PI at Baseline



Source: Johnson M, et al. J Acquir Immun Defic Syndr. 2019;81:463-72.

Switch to Doravirine-TDF-3TC versus Continued Baseline Regimen DRIVE SHIFT: Summary

Conclusions: “Switching to once-daily doravirine-lamivudine-tenofovir disoproxil fumarate is a generally well-tolerated option for maintaining viral suppression in patients considering a change in therapy.”

Source: Johnson M, et al. J Acquir Immun Defic Syndr. 2019;81:463-72.

Acknowledgments

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AETC AIDS Education & Training Center Program

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