National HIV Curriculum

Mini-Lecture Series

Bictegravir-Tenofovir alafenamide-Emtricitabine

Brian R. Wood, MD
Associate Editor, National HIV Curriculum
Associate Professor of Medicine
Division of Allergy and Infectious Diseases
University of Washington

Last Updated: July12, 2022

Disclosures

Dr. Wood has no financial conflicts of interest or disclosures.

Bictegravir-Tenofovir alafenamide-Emtricitabine

Bictegravir	Tenofovir alafenamide	Emtricitabine
50 mg	25 mg	200 mg
INSTI	NRTI	NRTI

Dose: 1 tablet once daily with or without food

Integrase Strand Transfer Inhibitors (INSTIs)

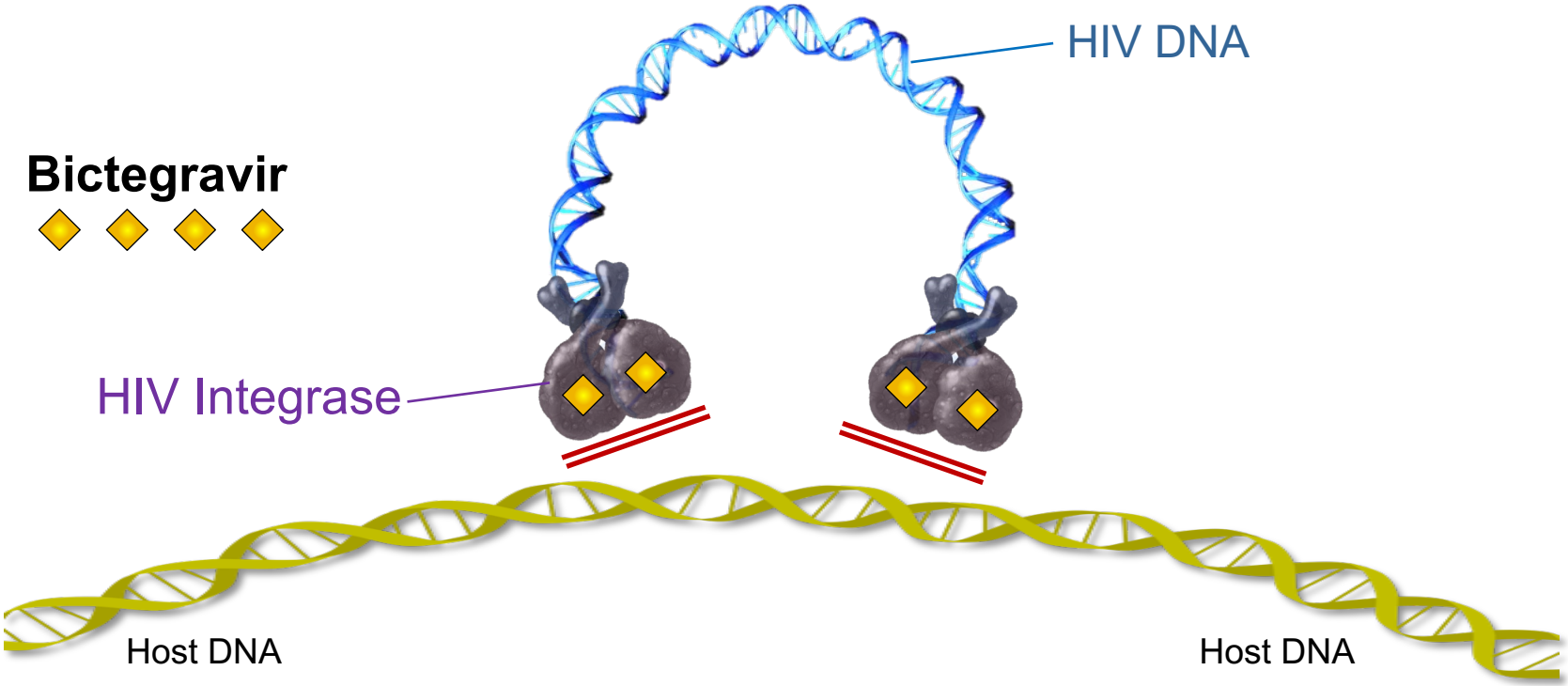


Illustration: *Cognition Studio, Inc.* and David H. Spach, MD

National HIV Curriculum

Nucleoside Reverse Transcriptase Inhibitors (NRTIs): Mechanism of Action

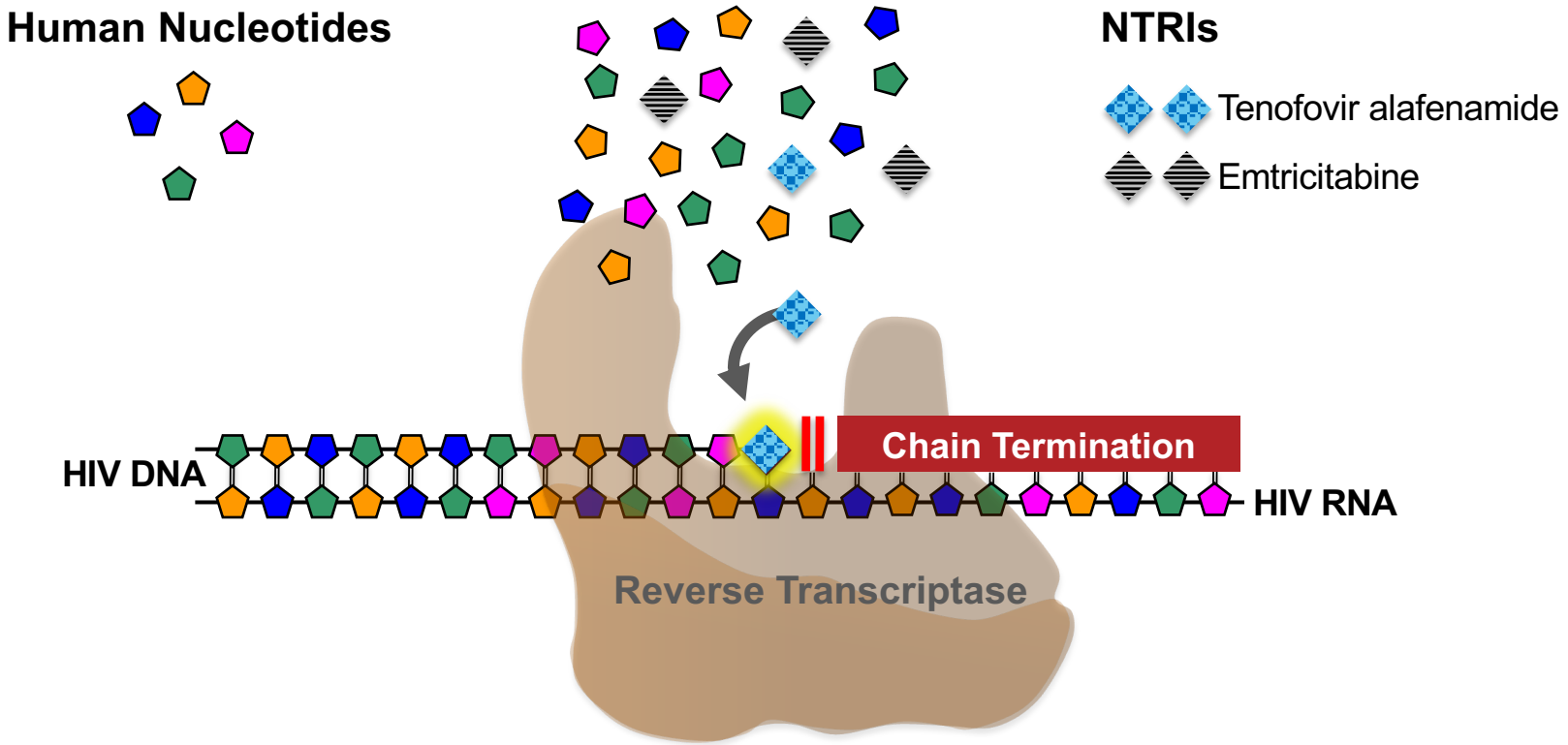


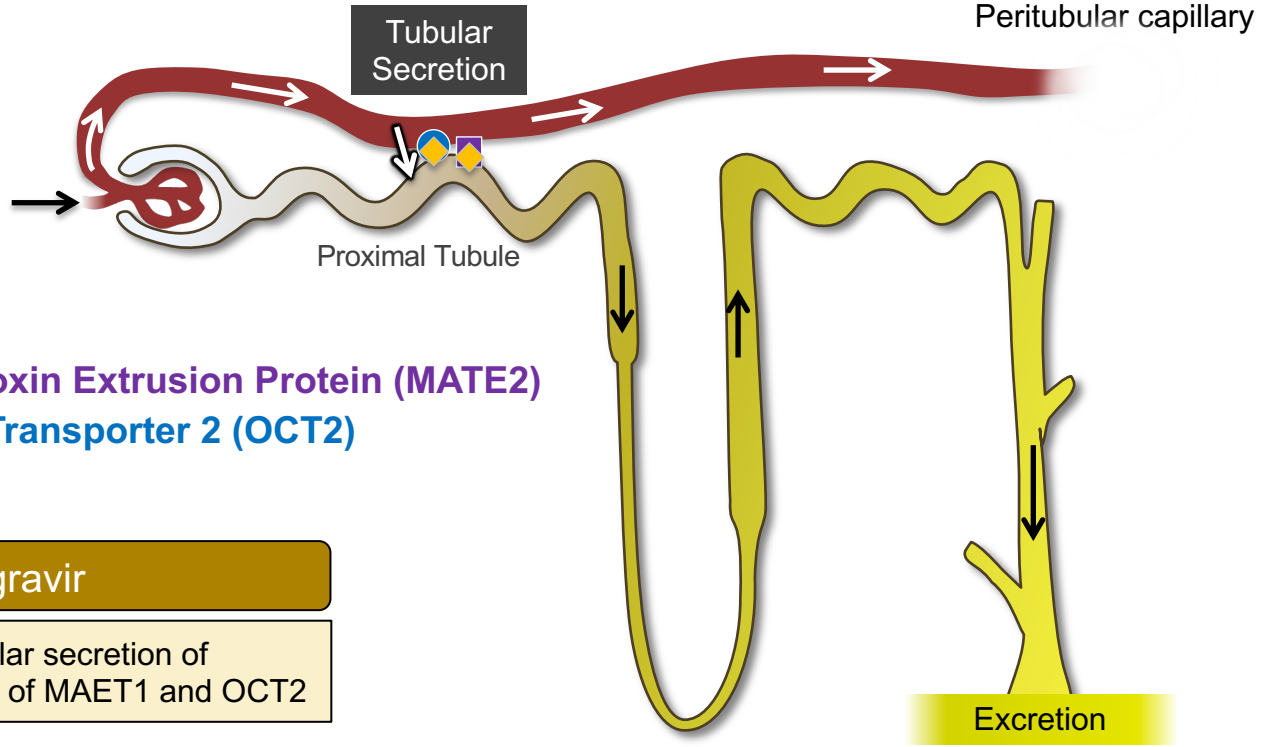
Illustration: David H. Spach, MD

Bictegravir-Tenofovir alafenamide-Emtricitabine

- **With Renal Impairment:** do not initiate if estimated CrCl <30 mL/min
- **Pregnancy**: insufficient data
- **Common Adverse Events (≥5%)**
  - Diarrhea (6%)
  - Nausea (5%)
  - Headache (5%)
- **Drug-Drug Interactions**
  - Avoid: rifamycins, dofetilide, carbamazepine, phenytoin, St. John's wort
  - Consider: metformin, cation-containing compounds

Source: Bictegravir-Tenofovir alafenamide-Emtricitabine Prescribing Information.

Bictegravir and Inhibition of Tubular Secretion of Creatinine



- **Multidrug and Toxin Extrusion Protein (MATE2)**
- **Organic Cation Transporter 2 (OCT2)**
- **Bictegravir**

Bictegravir

Decreases tubular secretion of creatinine via inhibition of MAET1 and OCT2

Illustration: David H. Spach, MD

Key Studies

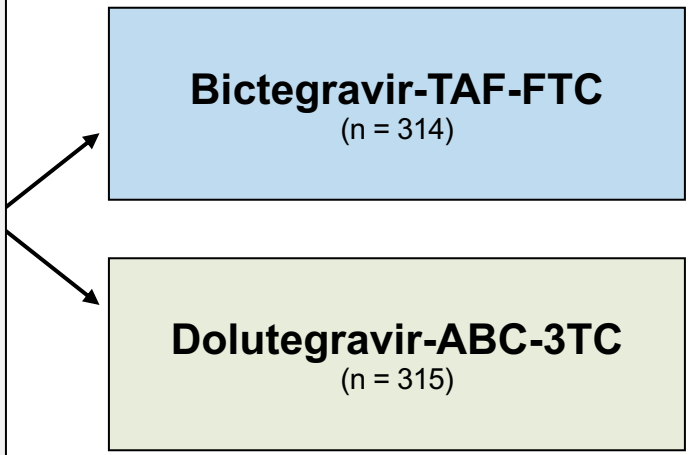
BIC-TAF-FTC vs. DTG-ABC-3TC as Initial Therapy

GS-380-1489: Week 48 Results

National HIV Curriculum

Bictegravir-TAF-FTC versus Dolutegravir-ABC-3TC as Initial Therapy GS-380-1489: Design

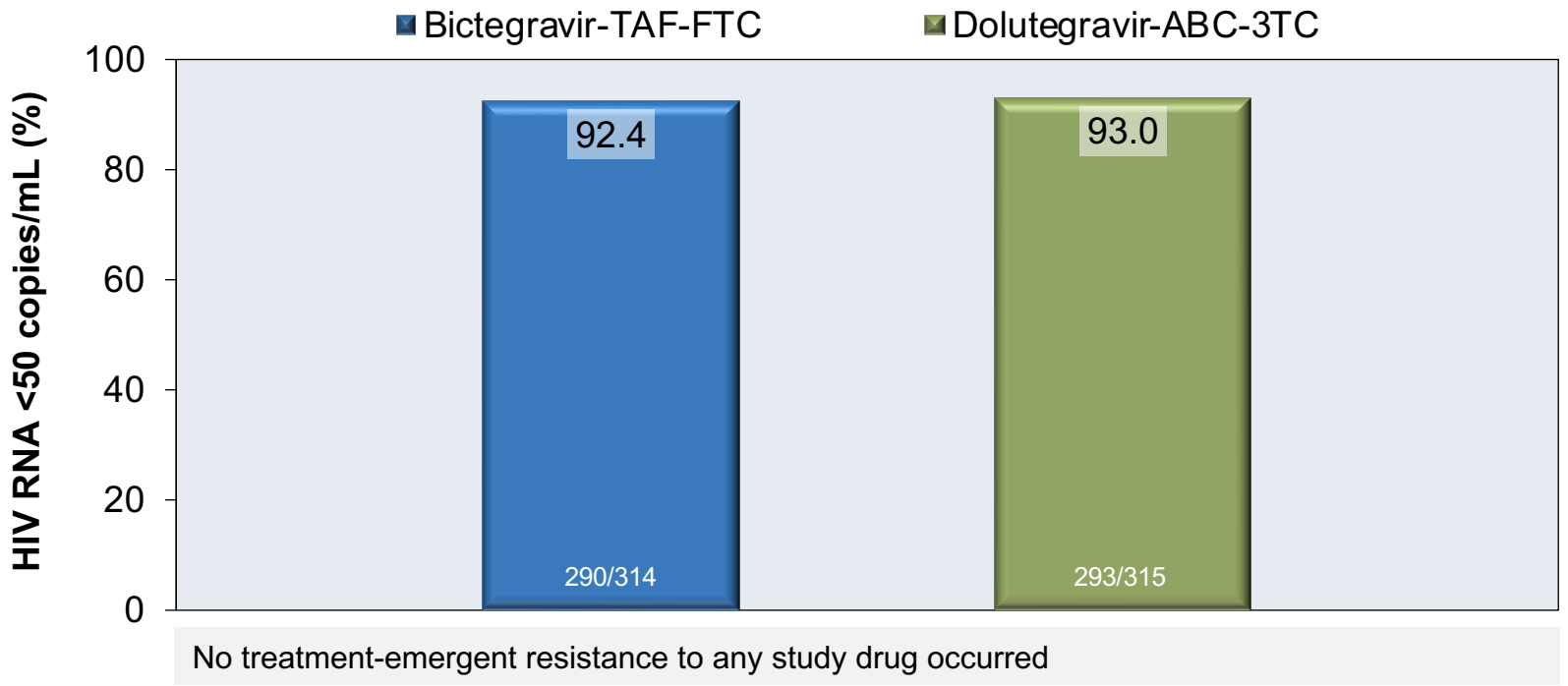
- **Design**
  - Randomized, double-blind, active-controlled, phase 3 study evaluating the efficacy and safety of bictegravir-tenofovir alafenamide-emtricitabine versus dolutegravir-abacavir-lamivudine for treatment-naïve adults with HIV
- **Including Criteria**
  - Age ≥18
  - Antiretroviral-naïve (or ≤10 days of treatment)
  - HIV RNA ≥500 copies/mL
  - eGFR ≥50 mL/min
  - HLA-B*5701 negative
  - No chronic HBV infection



Source: Gallant J, et al. Lancet. 2017;390:2063-72.

Bictegravir-TAF-FTC versus Dolutegravir-ABC-3TC as Initial Therapy GS-380-1489: Week 48 Results

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



No treatment-emergent resistance to any study drug occurred

Source: Gallant J, et al. Lancet. 2017;390:2063-72.

Bictegravir-TAF-FTC versus Dolutegravir-ABC-3TC as Initial Therapy GS-380-1489: Adverse Events

Treatment Emergent Adverse Events (AE's >5%) Through Week 48		
Adverse Effect	**BIC-TAF-FTC** (n = 314)	**DTG-ABC-3TC** (n = 315)
Diarrhea, %	13	13
Headache, %	11	14
Nausea, %	10	23
Fatigue, %	6	9
Arthralgia, %	4	6
Insomnia, %	4	6
Change in eGFR (mL/min)	-10.5	-10.8

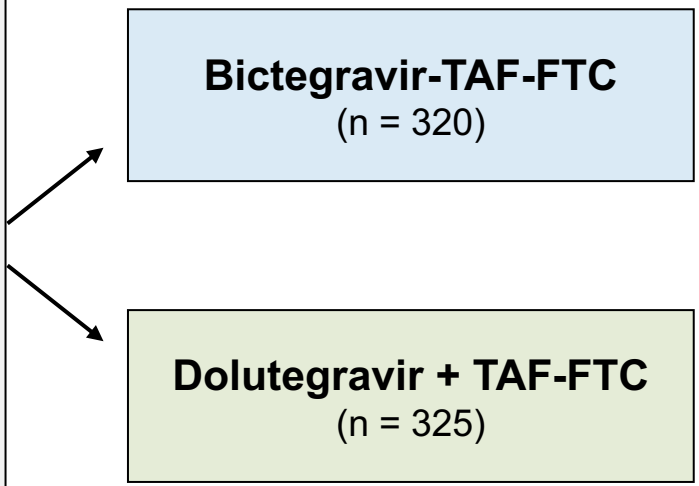
Source: Gallant J, et al. Lancet. 2017;390:2063-72.

BIC-TAF-FTC versus DTG + TAF-FTC as Initial Therapy

GS-380-1490: Week 48 Results

Bictegravir-TAF-FTC versus Dolutegravir + TAF-FTC as Initial Therapy GS-380-1490: Design

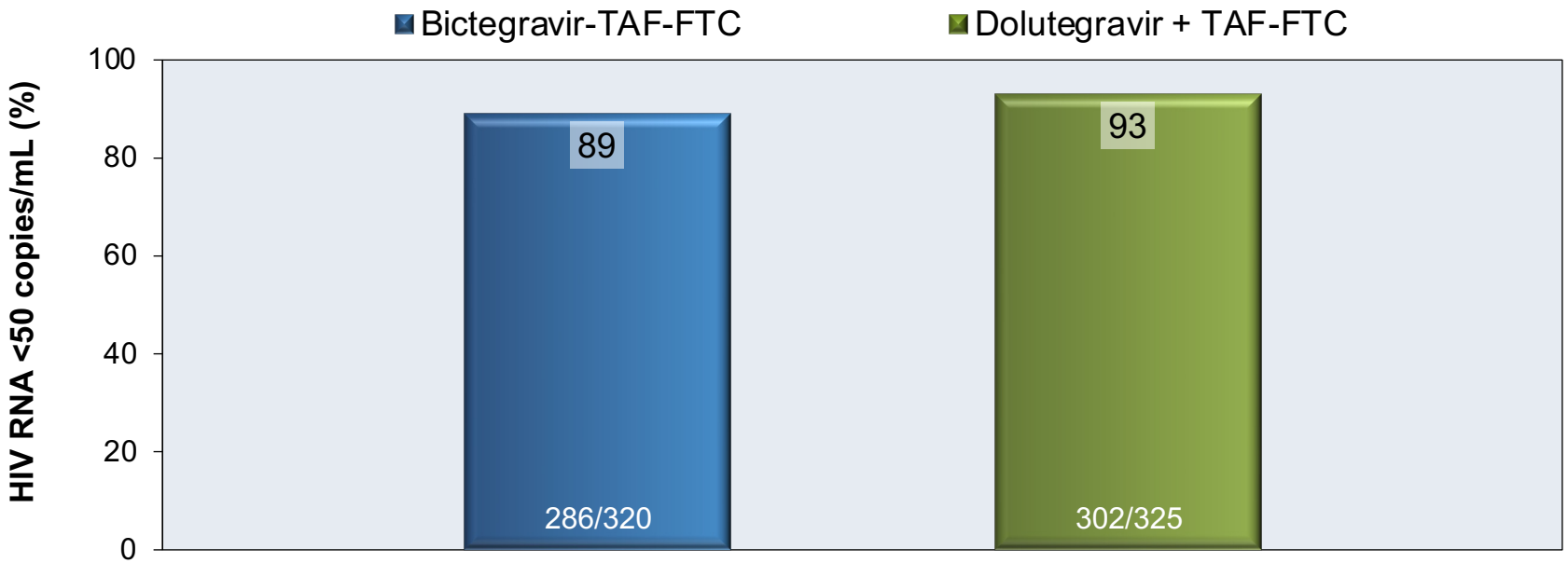
- **Design**
  - Randomized, double-blind, active-controlled, phase 3 study comparing bictegravir-tenofovir alafenamide-emtricitabine versus dolutegravir plus tenofovir alafenamide-emtricitabine as initial therapy
- **Inclusion Criteria**
  - Age ≥18 years
  - Antiretroviral-naïve (or ≤10 days of treatment)
  - HIV RNA ≥500 copies/mL
  - eGFR ≥30 mL/min



Source: Sax PE, et al. Lancet. 2017;390:2073-82.

Bictegravir-TAF-FTC versus Dolutegravir + TAF-FTC as Initial Therapy GS-380-1490: Week 48 Results

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



No participant discontinued due to lack of efficacy in either arm
No treatment-emergent resistance to any study drug occurred

Source: Sax PE, et al. Lancet. 2017;390:2073-82.

Bictegravir-TAF-FTC versus Dolutegravir + TAF-FTC as Initial Therapy GS-380-1490: Adverse Events

Treatment Emergent Adverse Events (AE's >5%) Through Week 48		
	BIC-TAF-FTC (n = 320)	**DTG + TAF-FTC** (n = 325)
Headache, %	13	12
Diarrhea, %	12	12
Nausea, %	8	9
Fatigue, %	6	8
Arthralgia, %	5	3
Insomnia, %	5	4
Change in eGFR	-7.3 mL/min	-10.8 mL/min

Abbreviations: eGFR = estimated glomerular filtration

Source: Sax PE, et al. Lancet. 2017;390:2073-82.

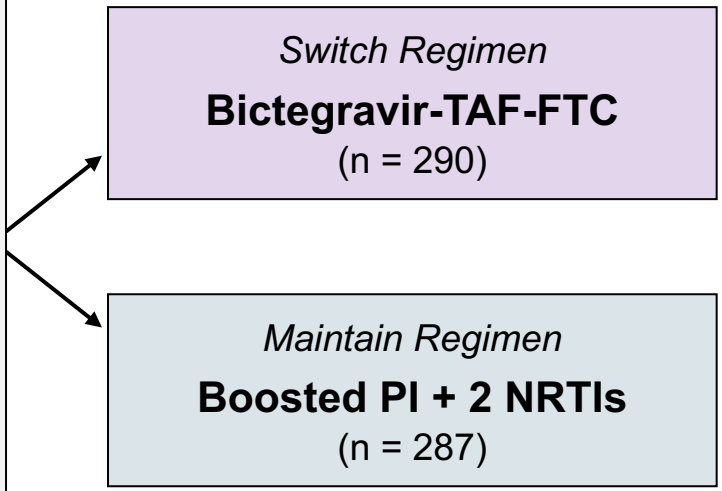
Switch from Boosted PI + 2 NRTIs to BIC-TAF-FTC with Viral Suppression

GS-380-1878

National HIV Curriculum

Switch from Boosted PI + 2 NRTIs to Bictegravir-TAF-FTC GS-380-1878: Design

- **Background**
  - Randomized, phase 3, multicenter, open-label switch study evaluating the efficacy and safety of switching adults with viral suppression taking a boosted PI plus 2 NRTIs to BIC-TAF-FTC
- **Inclusion Criteria**
  - Age ≥18 years
  - HIV RNA <50 copies/mL for ≥6 months
  - Taking stable antiretroviral regimen for ≥6 months
  - No history of virologic failure
  - No prior treatment with an INSTI
  - eGFR ≥50 mL/min
  - HBV and HCV allowed
  - Taking atazanavir or darunavir (each boosted by ritonavir or cobicistat) + TDF-FTC or ABC-3TC



Source: Daar E, et al. Lancet HIV. 2018;5:e347-e356.

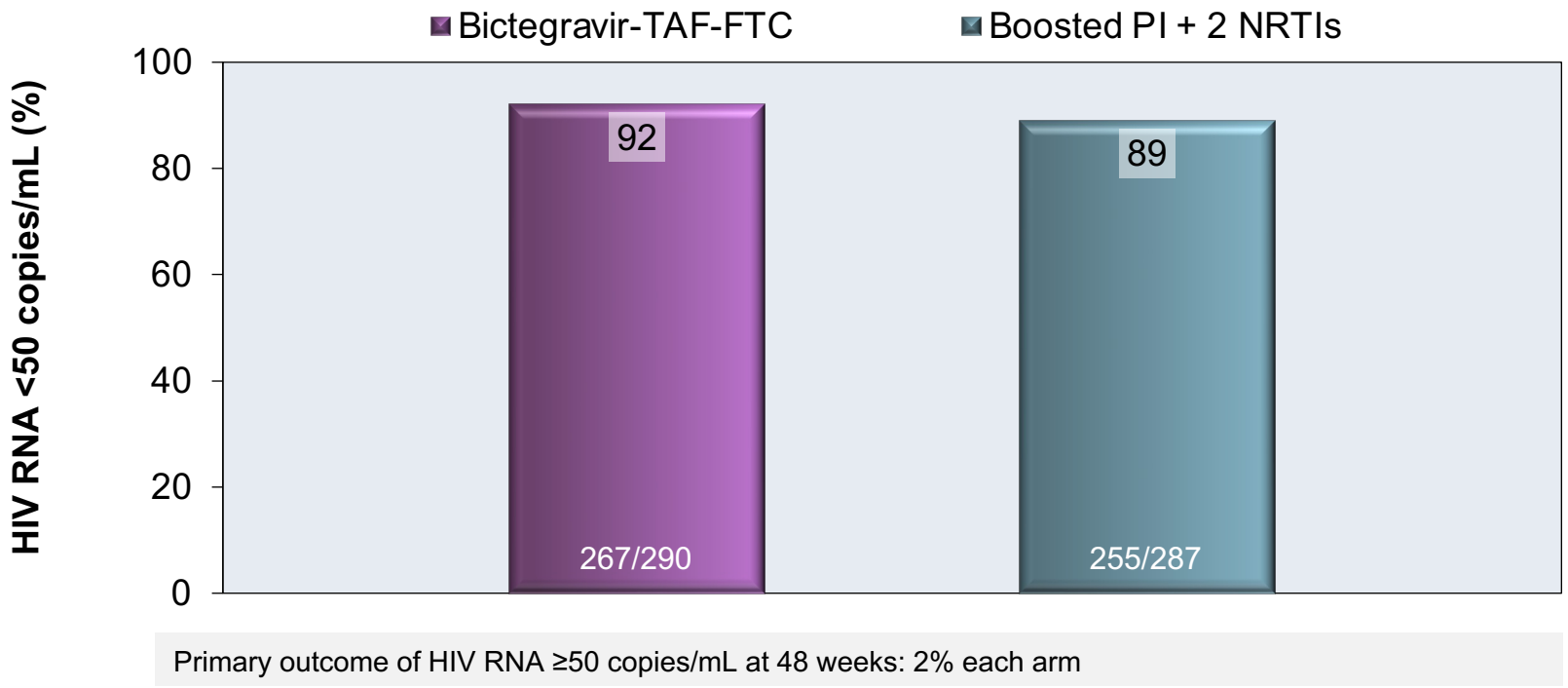
Switch from Boosted PI + 2 NRTIs to Bictegravir-TAF-FTC
GS-380-1878: Baseline Characteristics

Study GS-380-1878 Baseline Antiretroviral Regimen		
Baseline Antiretroviral Medications	**BIC-TAF-FTC** (n = 290)	**Boosted PI + 2 NRTIs** (n = 287)
NRTI		
Tenofovir DF-emtricitabine, %	84	85
Abacavir-lamivudine, %	16	15
Protease Inhibitor	21	16
Darunavir, %	57	54
Atazanavir, %	43	46

Source: Daar E, et al. Lancet HIV. 2018;5:e347-e356.

Switch from Boosted PI + 2 NRTIs to Bictegravir-TAF-FTC GS-380-1878: Results

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

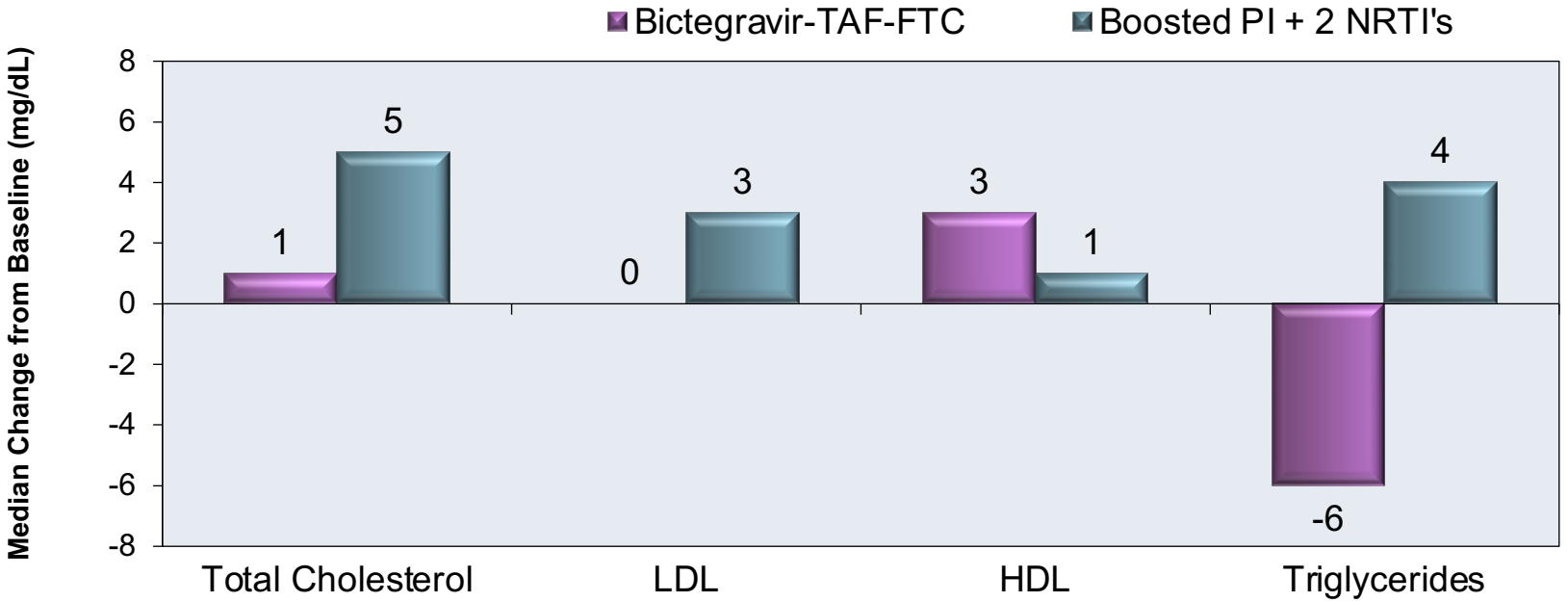


Primary outcome of HIV RNA ≥50 copies/mL at 48 weeks: 2% each arm

Source: Daar E, et al. Lancet HIV. 2018;5:e347-e356.

Switch from Boosted PI + 2 NRTIs to Bictegravir-TAF-FTC GS-380-1878: Results

Change in Lipids at 48 Weeks



Source: Daar E, et al. Lancet HIV. 2018;5:e347-e356.

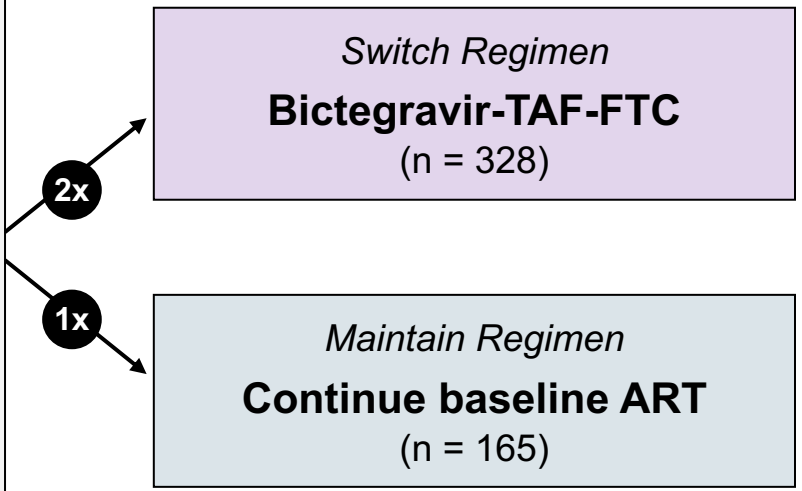
Switch to Bictegravir-Tenofovir alafenamide-Emtricitabine for Black Americans

BRAAVE2020

National HIV Curriculum

Switch to Bictegravir-TAF-FTC for Black Americans
BRAAVE2020: Design

- **Background**
  - Randomized, phase 3, multicenter, open-label switch study evaluating the efficacy and safety of switching Black American adults with viral suppression to BIC-TAF-FTC, including individuals with a history of NRTI, NNRTI, and/or PI resistance
- **Inclusion Criteria**
  - Age ≥18 years
  - Self-described as Black, African American, or mixed race that includes Black
  - HIV RNA <50 copies/mL for ≥12 months
  - Taking stable antiretroviral regimen that includes 2 NRTIs plus 3rd agent for ≥6 months
  - eGFR ≥50 mL/min
  - No INSTI resistance; no K65R, T69ins, or ≥3TAMs

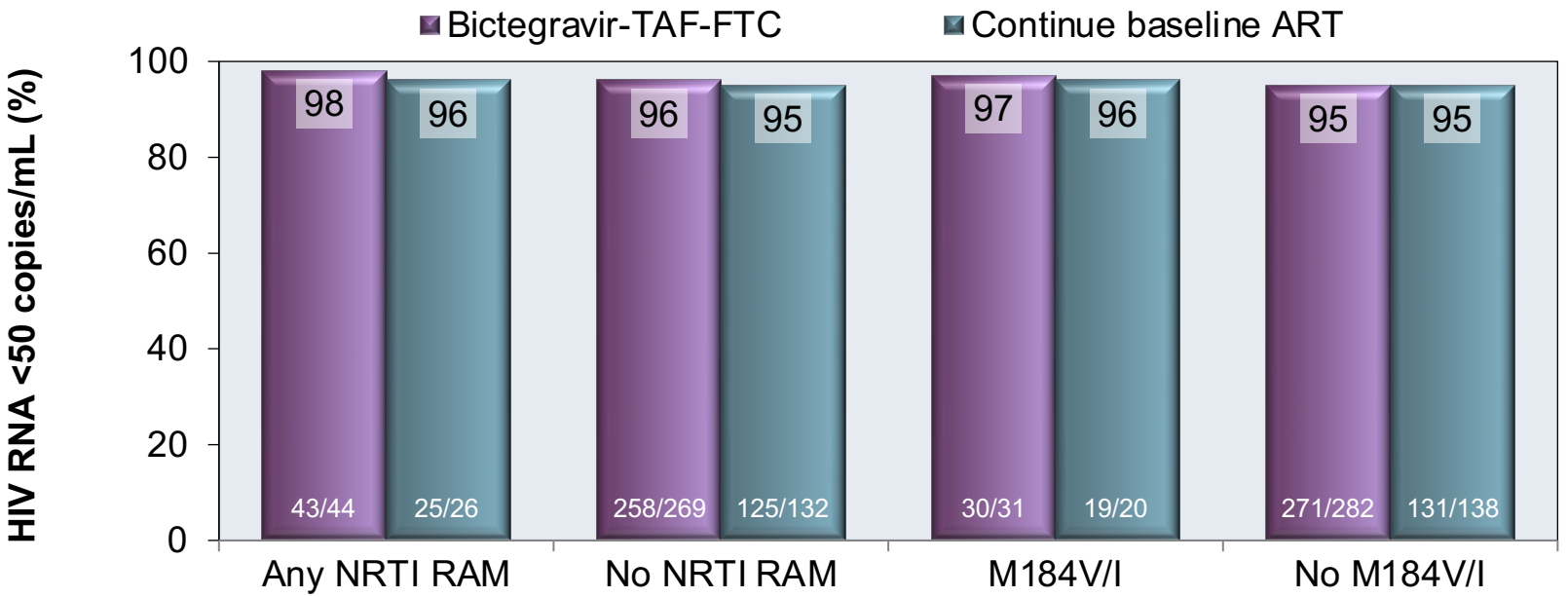


10% of all participants with M184V at baseline

Source: Haggins D, et al. JAIDS. 2021;88:86-95.

Switch to Bictegravir-TAF-FTC for Black Americans
BRAAVE2020: Results

Week 24 Virologic Response by Baseline Resistance (Intention-to-Treat Analysis)



RAM = resistance-associated mutation

Source: Haggins D, et al. JAIDS. 2021;88:86-95.

Resistance Development on Bictegravir-TAF-FTC

- Treatment-emergent resistance described in individuals who develop virologic failure on BIC-TAF-FTC, but rare
- Resistance testing requires standard (RT/PR) and integrase genotype
- Most common emergent mutations: R263K (integrase), M184V (RT)
- R263K confers low-to-intermediate resistance to all INSTIs
- With virologic rebound on BIC-TAF-FTC the genotypes more often show no new resistance mutations and the regimen remains active

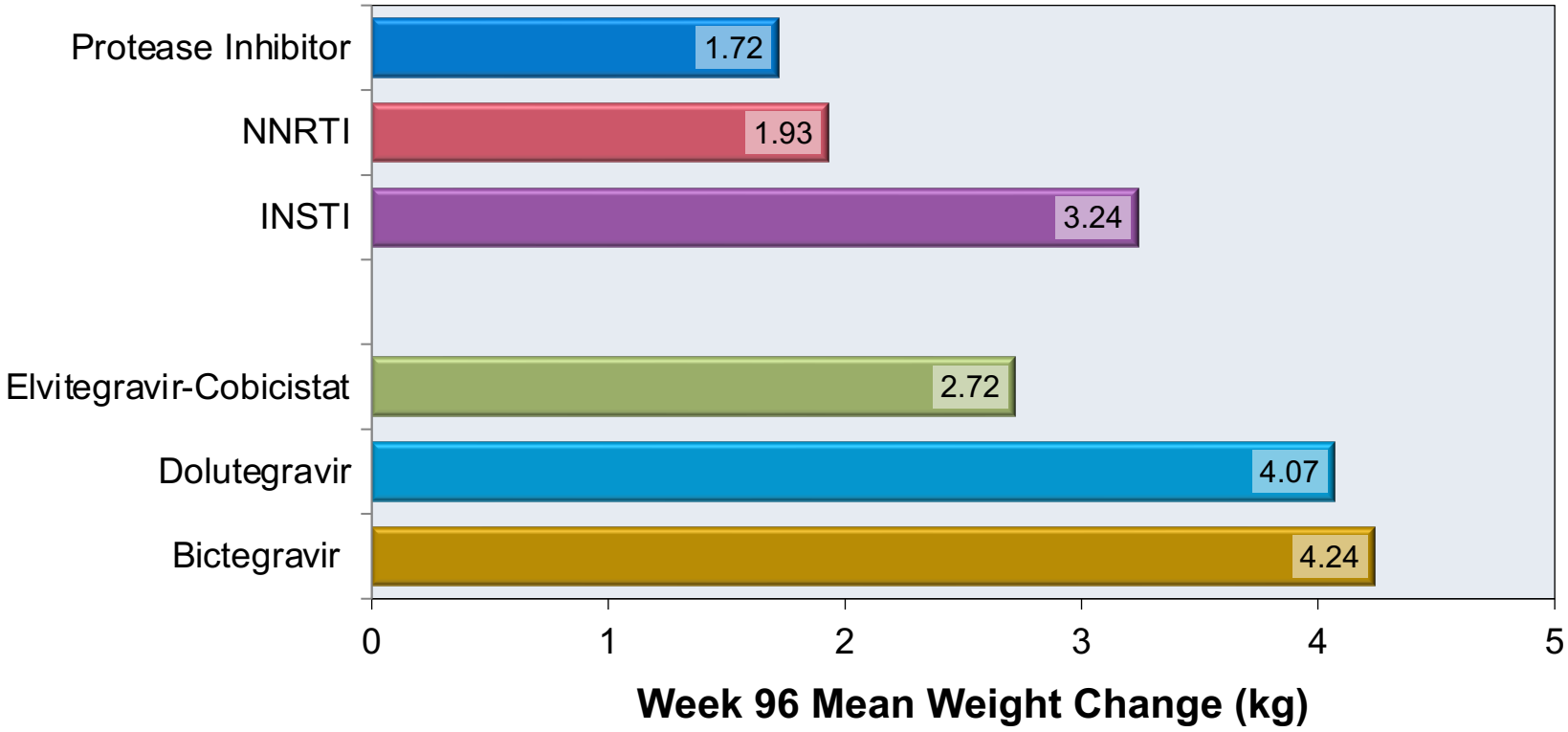
Sources:
Chamberlain N, et al. OFID. 2021;8:ofab297.
Lozano AB, et al. Antiviral Res. 2020;179:104717.

Weight Change with Bictegravir-TAF-FTC

- After ART initiation, greater weight gain observed with bictegravir (or dolutegravir) as compared to other options, especially when combined with TAF
- Switching from an NNRTI or boosted PI to bictegravir (or dolutegravir) may lead to weight gain, especially if also switching an alternate NRTI to TAF
- Weight gain with initial therapy or switch generally plateaus after 6 to 12 months
- Several mechanisms have been proposed but not confirmed
- Long-term metabolic and cardiovascular consequences also require further study

Source:
Ruderman SA, et al. JAIDS. 2021;86:339-43.
Sax PE, et al. Clin Infect Dis. 2020;71:1379-89.
Erlandson KM, et al. Clin Infect Dis. 2021;73:1440-51.
Wood BR, Huhn GD. OFID. 2021;8:ofab542.

Weight Gain on Antiretroviral Regimens



Source: Sax PE, et al. Clin Infect Dis. 2020;71:1379-89.

Bictegravir-Tenofovir alafenamide-Emtricitabine: Summary

- Oral, once-daily, single-tablet regimen
- First-line option for initial ART
- Frequently used switch option if no significant INSTI resistance and limited or no NRTI resistance (M184V/I mutation ok; usually avoid with K65R or ≥3 TAMs)
- May artificially raise serum creatinine and may lead to more weight gain than non-INSTI options
- Some drug-drug interactions exist, including with cation-containing compounds (which may be over-the-counter)
- May be combined with other antiretrovirals as part of salvage ART

Acknowledgments

The production of this **National HIV Curriculum** Mini-Lecture was supported by Grant U1OHA32104 from the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS). Its contents are solely the responsibility of University of Washington IDEA Program and do not necessarily represent the official views of HRSA or HHS.

AETC AIDS Education & Training Center Program

National HIV Curriculum

IDEA INFECTIOUS DISEASES EDUCATION & ASSESSMENT