National HIV Curriculum

Mini-Lecture Series

Dolutegravir-Abacavir-Lamivudine

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Disclosures

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Dolutegravir-Abacavir-Lamivudine (DTG-ABC-3TC)

Dolutegravir	Abacavir	Lamivudine
50 mg	600 mg	300 mg
INSTI	NRTI	NRTI

Dose: 1 tablet once daily with or without food

Dolutegravir-Abacavir-Lamivudine Single-Tablet Regimen

- **Indication**
  - Complete regimen for treatment of HIV-1 in persons weighing ≥ 25 kg:
    - No known substitutions associated with resistance to dolutegravir, *and*
    - Do NOT have HLA-B*5701 allele
- **Testing Prior to Initiation**
  - HLA-B*5701 allele testing
  - Serologic testing for hepatitis B (HBV) virus infection
- **With Renal or Hepatic Impairment**
  - Not recommended if estimated CrCl <30 mL/min
  - Not recommended with mild hepatic impairment (Child-Pugh A)

Dolutegravir-Abacavir-Lamivudine: Mechanism of Action

Nucleoside Reverse Transcriptase Inhibitors (NRTIs): Mechanism of Action

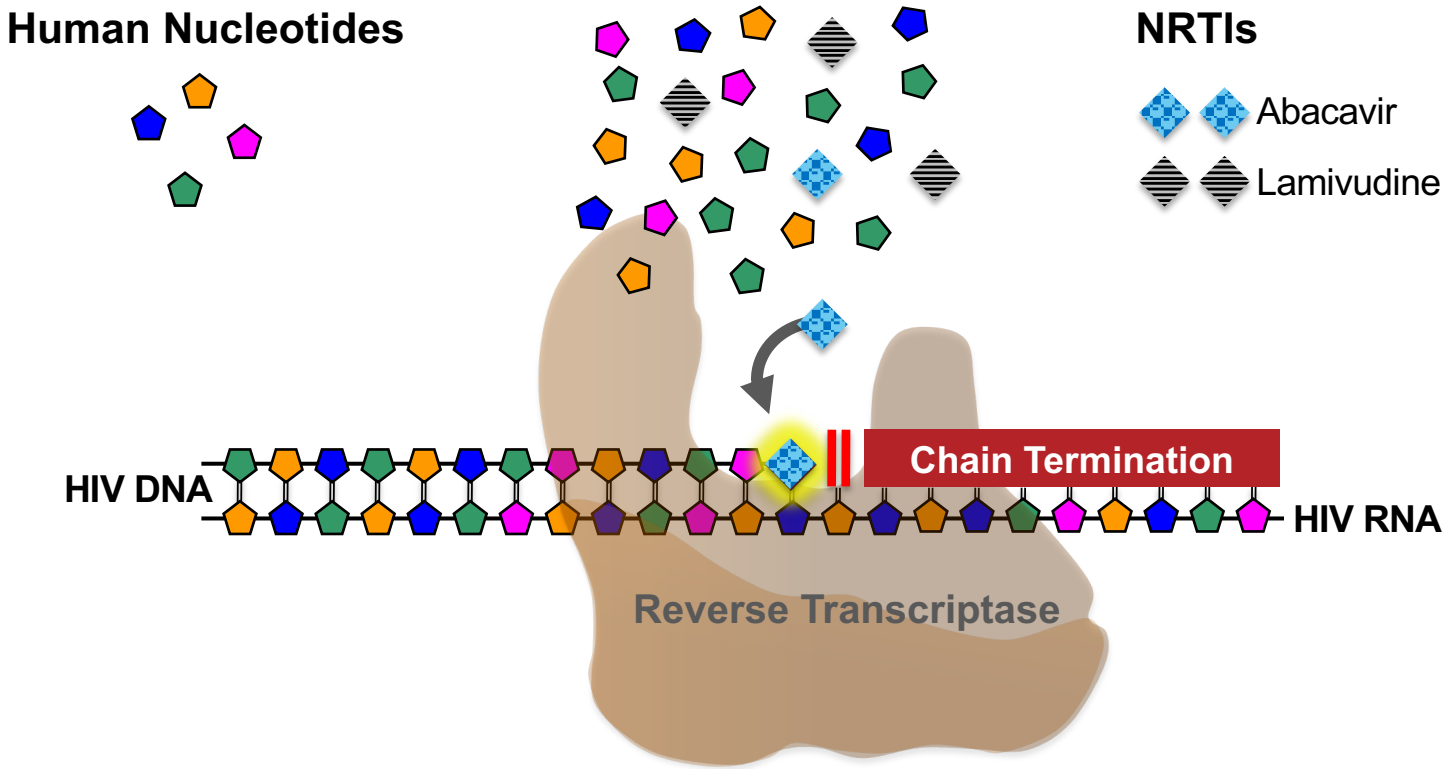

Illustration: David H. Spach, MD

Integrase Strand Transfer Inhibitors (INSTIs): Mechanism of Action

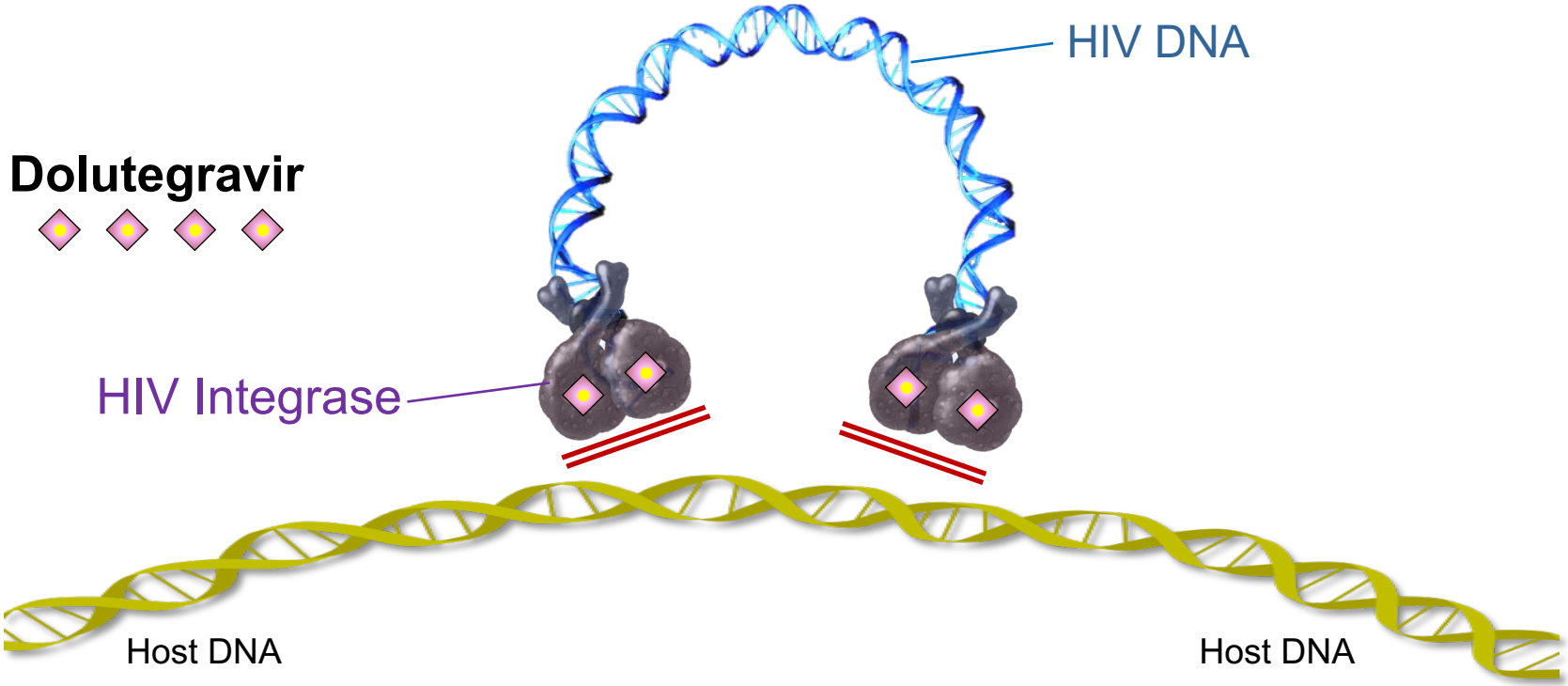

Illustration: *Cognition Studio, Inc.* and David H. Spach, MD

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Key Clinical Trials

Dolutegravir-Abacavir-Lamivudine
Summary of Key Studies

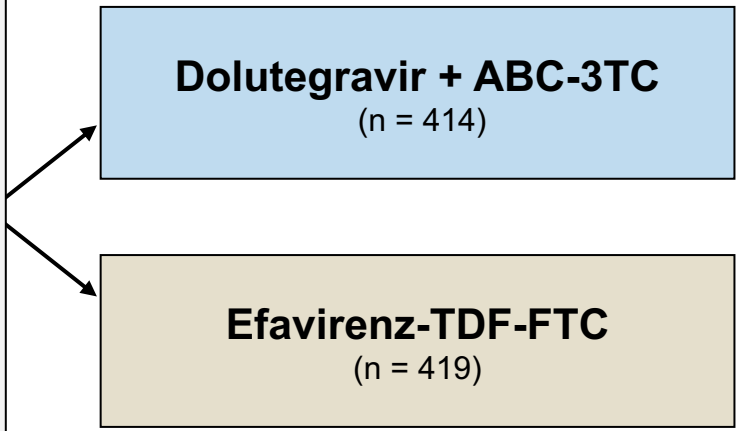
- **Trials in Treatment Naïve Adults**
  - SINGLE[1]: DTG + ABC-3TC versus EFV-TDF-FTC
  - GS-380-1489[2]: BIC-TAF-FTC versus DTG-ABC-3TC

- **Trials In Adults with Virologic Suppression**
  - STRIVIING[3]: Switch to DTG-ABC-3TC or stay on baseline ART

Source: [1]Walmsley SL, et al. N Engl J Med. 2013;369;1807-18. [2] Gallant J, et al. Lancet. 2017;390:2063-72. [3]Trottier B, et al. Antivir Ther. 2017;22:295-305.

Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC SINGLE Study: Design

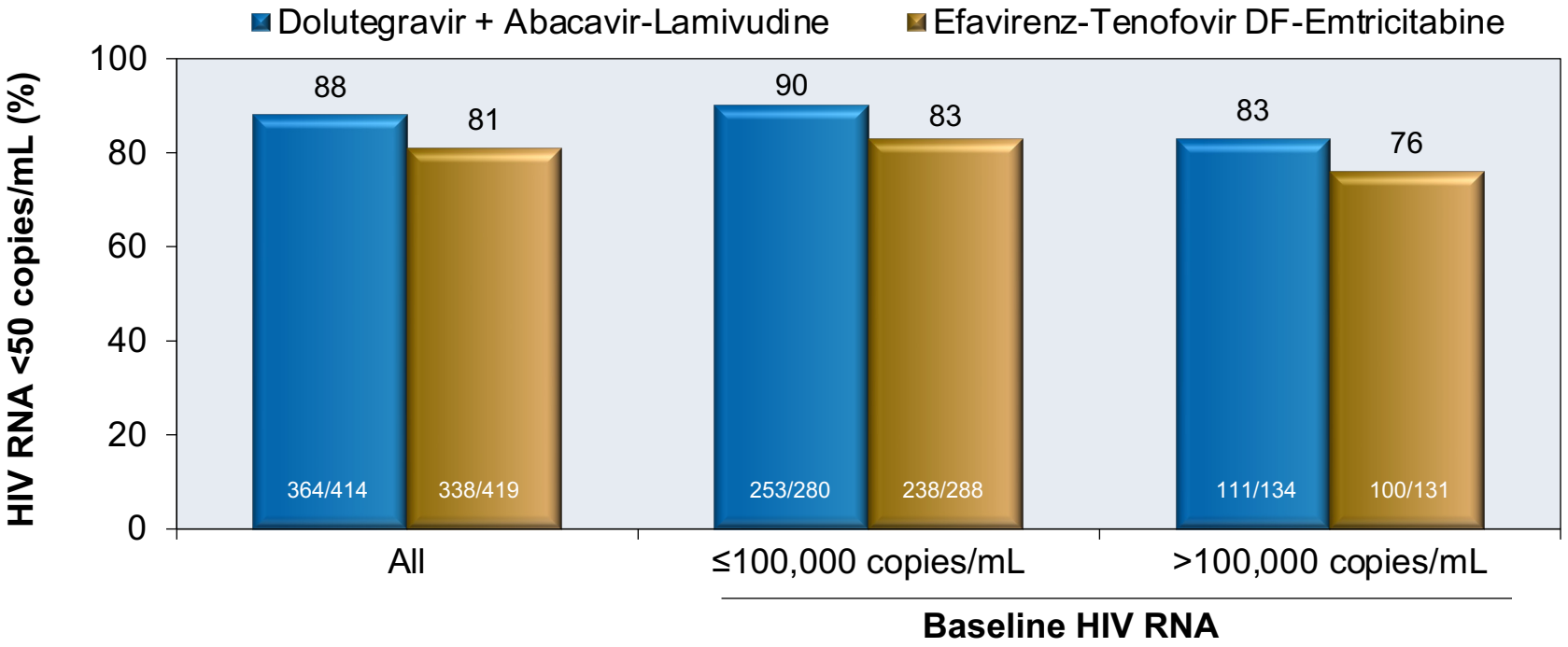
- **Background**:
  - Randomized, double-blind study, phase 3 trial comparing dolutegravir + abacavir-lamivudine with efavirenz-tenofovir DF-emtricitabine
- **Inclusion Criteria (n = 833)**
  - Antiretroviral-naïve adults
  - Age ≥18 years
  - HIV RNA ≥1,000 copies/mL
  - No active CDC AIDS condition
- **Treatment Arms**
  - Dolutegravir (QD) + Abacavir-lamivudine
  - Efavirenz-Tenofovir DF-Emtricitabine



Source: Walmsley SL, et al. N Engl J Med. 2013;369;1807-18.

Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC SINGLE Study: Result

Week 48 Virologic Response (ITT Analysis)



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Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC SINGLE Study: Result

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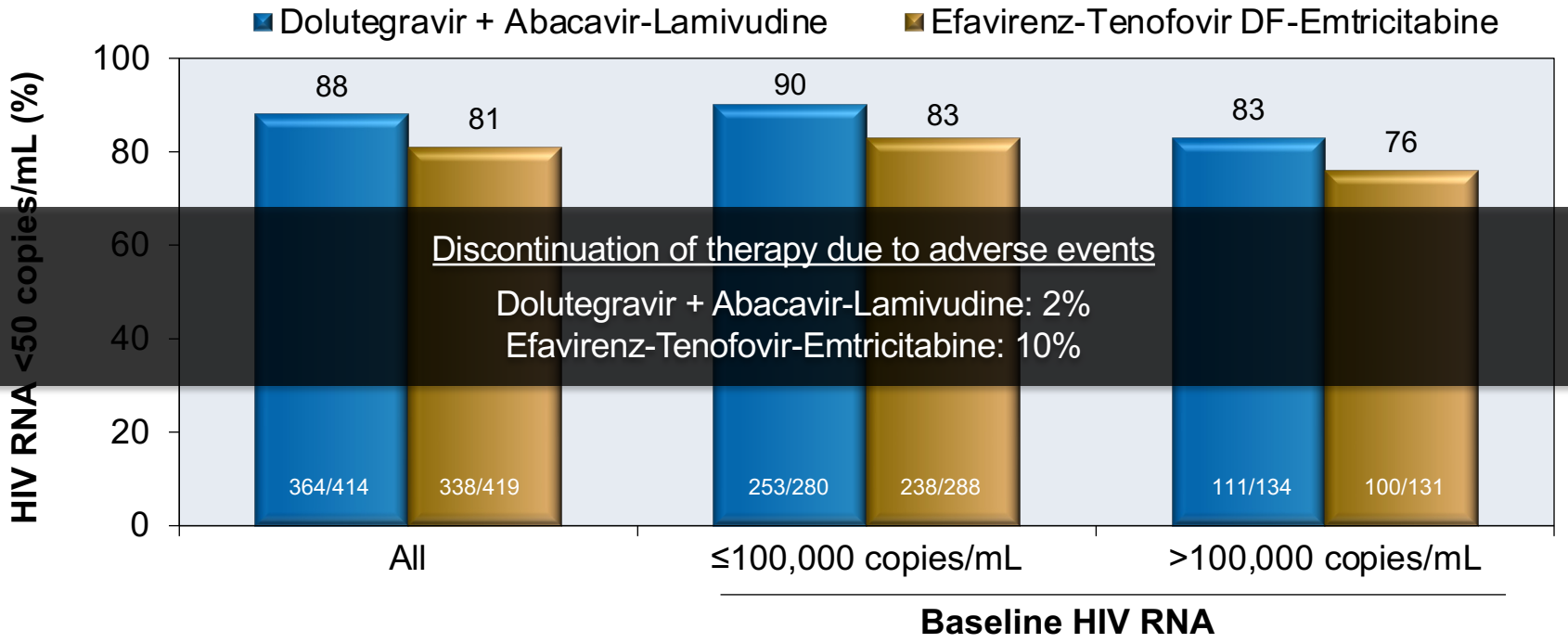

Source: Walmsley SL, et al. N Engl J Med. 2013;369;1807-18.

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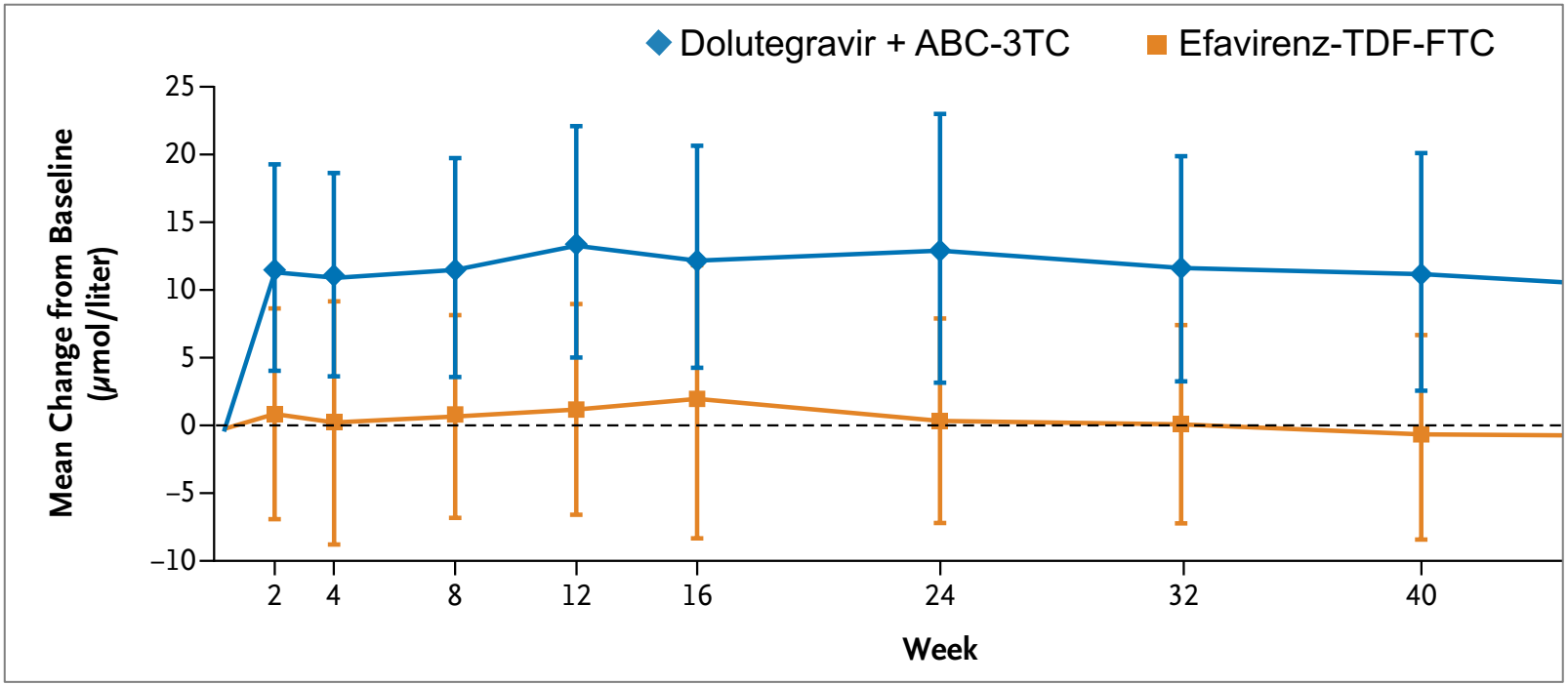
Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC SINGLE Study: Result

Mean Change from Baseline in Serum Creatinine Levels



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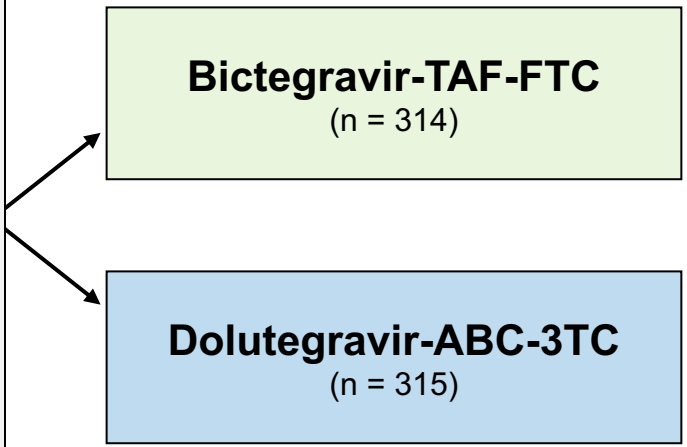
BIC-TAF-FTC versus DTG-ABC-3TC as Initial Therapy
GS-380-1489: Design

- **Background**
  - 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
- **Inclusion Criteria**
  - Age >18 years
  - Antiretroviral-naïve (or ≤10 days of treatment)
  - HIV RNA ≥500 copies/mL
  - eGFR ≥50 mL/min
  - HLA B*5701 negative
  - No chronic HBV infection
- **Regimens**
  - Bictegravir-TAF-FTC (50/25/200 mg)
  - Dolutegravir-ABC-3TC (50/600/300 mg)



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

BIC-TAF-FTC versus DTG-ABC-3TC as Initial Therapy
GS-380-1489: Baseline Characteristics

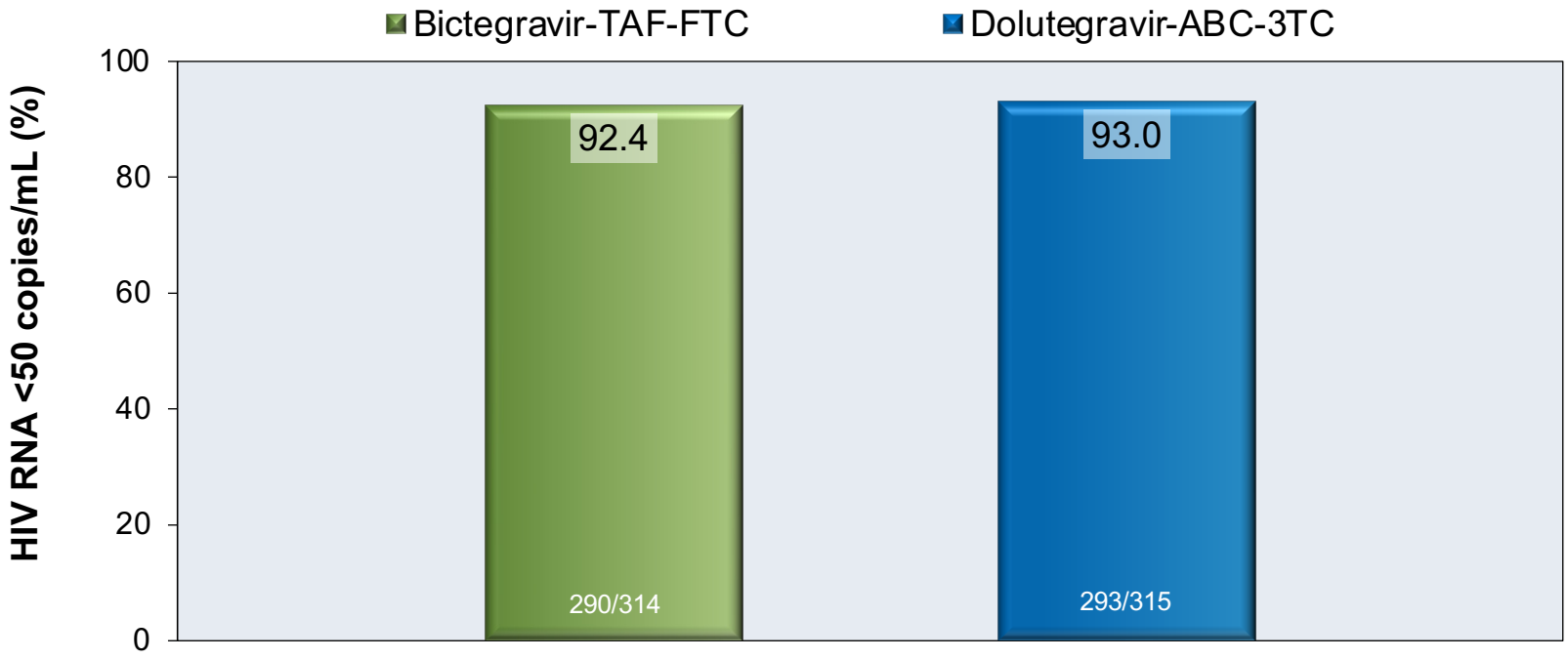
Study GS-380-1489 Baseline Characteristics		
Characteristic	**BIC-TAF-FTC** (n = 314)	**DTG-ABC-3TC** (n = 315)
Median age, years (range)	31 (18-71)	32 (18-68)
Male/Female, %	91/9	90/10
Black or African descent, %	36	36
HIV RNA >100,000 copies/mL, %	17	16
CD4 count <200 cells/mm^3, %	11	10
Median CrCl, mL/min	125.9	123.0

Abbreviations: CrCl = creatinine clearance

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

BIC-TAF-FTC versus DTG-ABC-3TC as Initial Therapy
GS-380-1489: Results

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



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BIC-TAF-FTC versus DTG-ABC-3TC as Initial Therapy
GS-380-1489: Results

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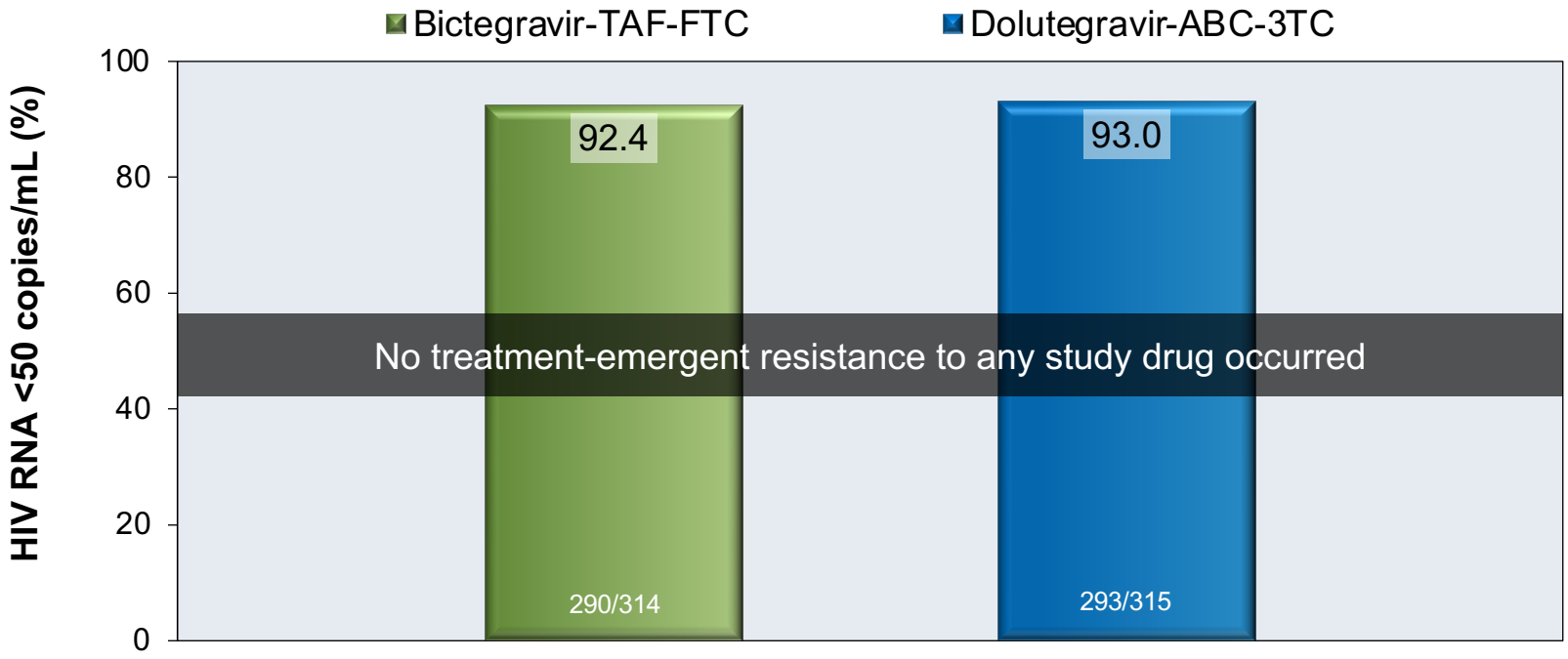


Source: Gallant J, et al. Lancet. 2017;390:2063-72.

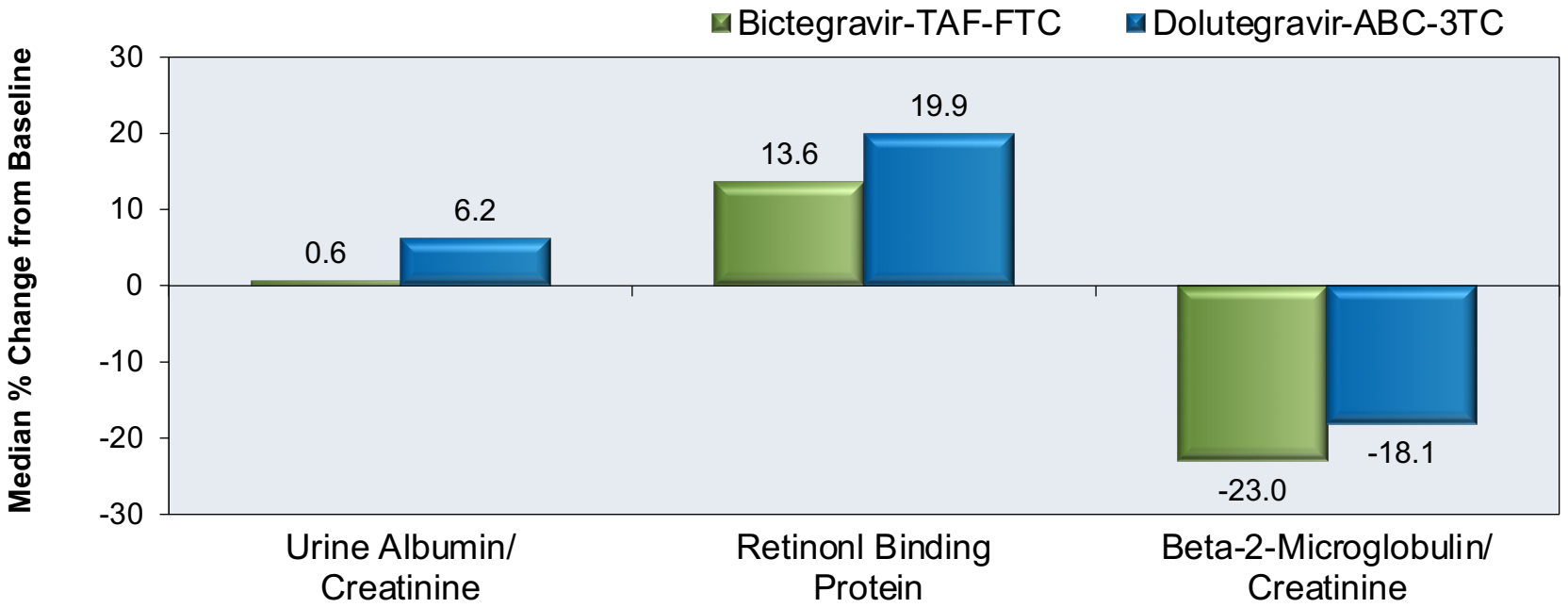
BIC-TAF-FTC versus DTG-ABC-3TC as Initial Therapy
GS-380-1489: Adverse Events

Treatment Emergent Adverse Events (AE's >5%) Through Week 48		
	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-ABC-3TC for Initial Therapy GS-380-1489: Results

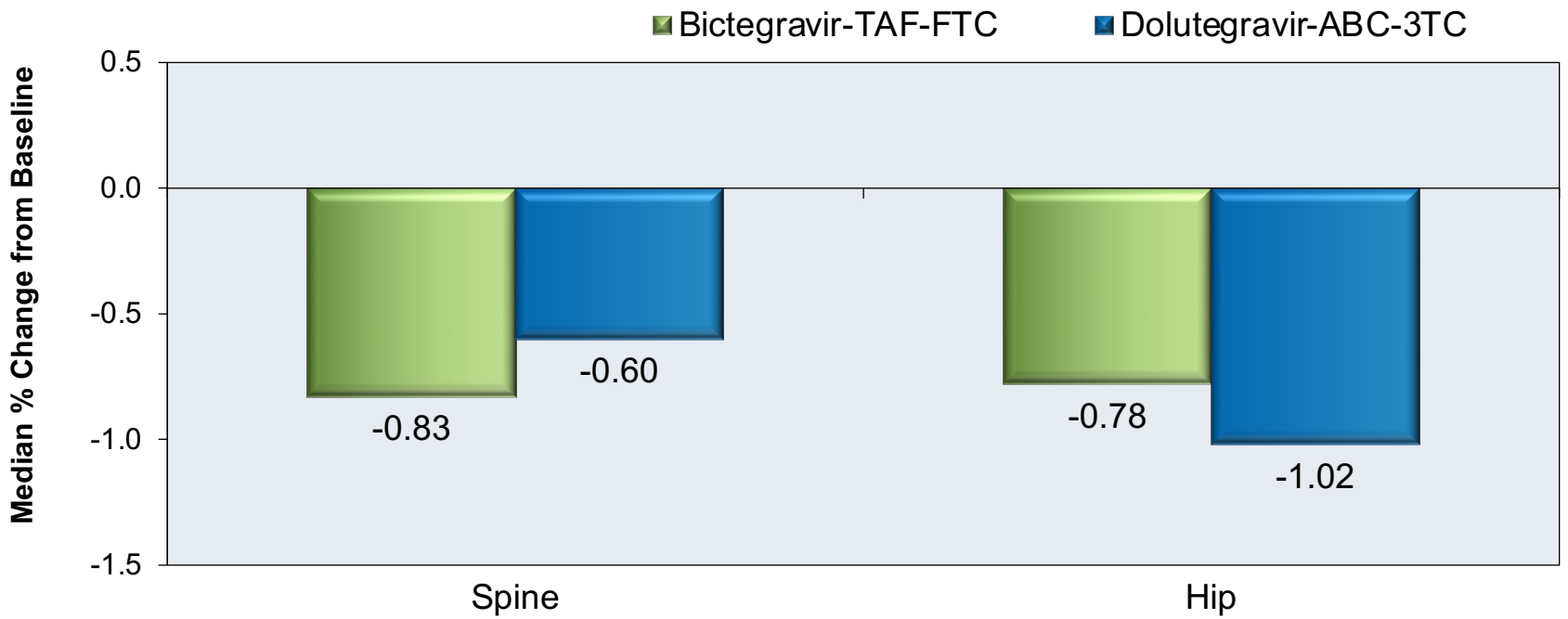
Change in Markers of Proximal Tubulopathy at 48 Weeks



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

BIC-TAF-FTC versus DTG-ABC-3TC for Initial Therapy GS-380-1489: Results

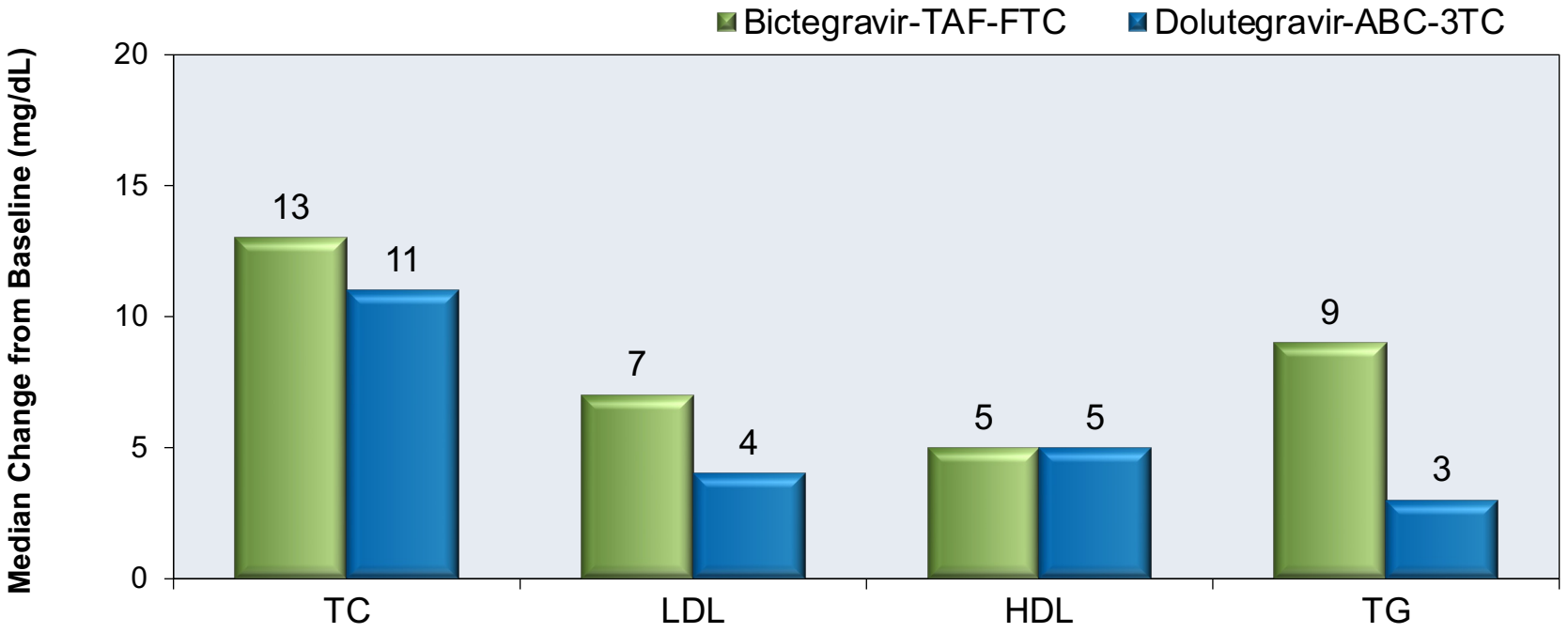
Change in Bone Mineral Density at 48 Weeks



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

BIC-TAF-FTC versus DTG-ABC-3TC for Initial Therapy
GS-380-1489: Results

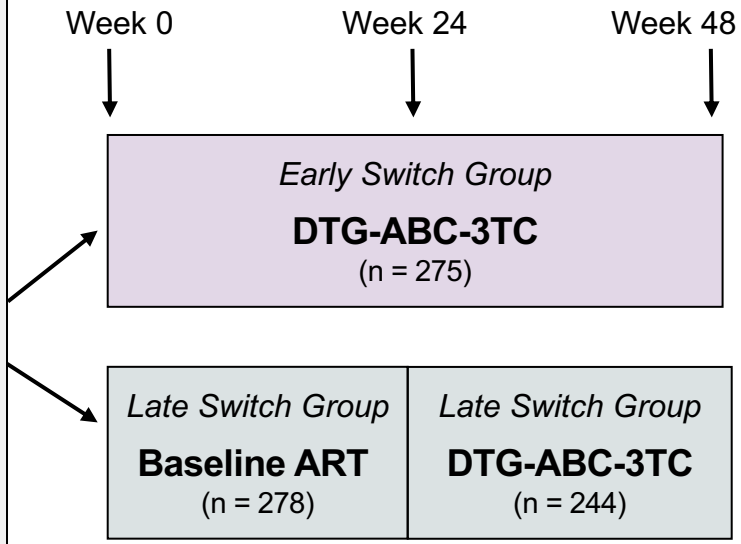
Change in Lipids at 48 Weeks



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

Switch to Dolutegravir-Abacavir-Lamivudine (DTG-ABC-3TC) STRIIVING: Design

- **Background**
  - Open-label, randomized study, phase 3 trial comparing switch to dolutegravir-abacavir-lamivudine (DTG-ABC-3TC) versus continuation of baseline ART
- **Inclusion Criteria** (n = 553)
  - HIV RNA <50 copies/mL on ART
  - Stable on current ART for ≥6 months
  - No prior virologic failure
  - HLA-B*5701 negative
- **Treatment Arms**
  - Switch to DTG-ABC-3TC
  - Continuation of Baseline ART x 24 weeks, then switch to DTG-ABC-3TC

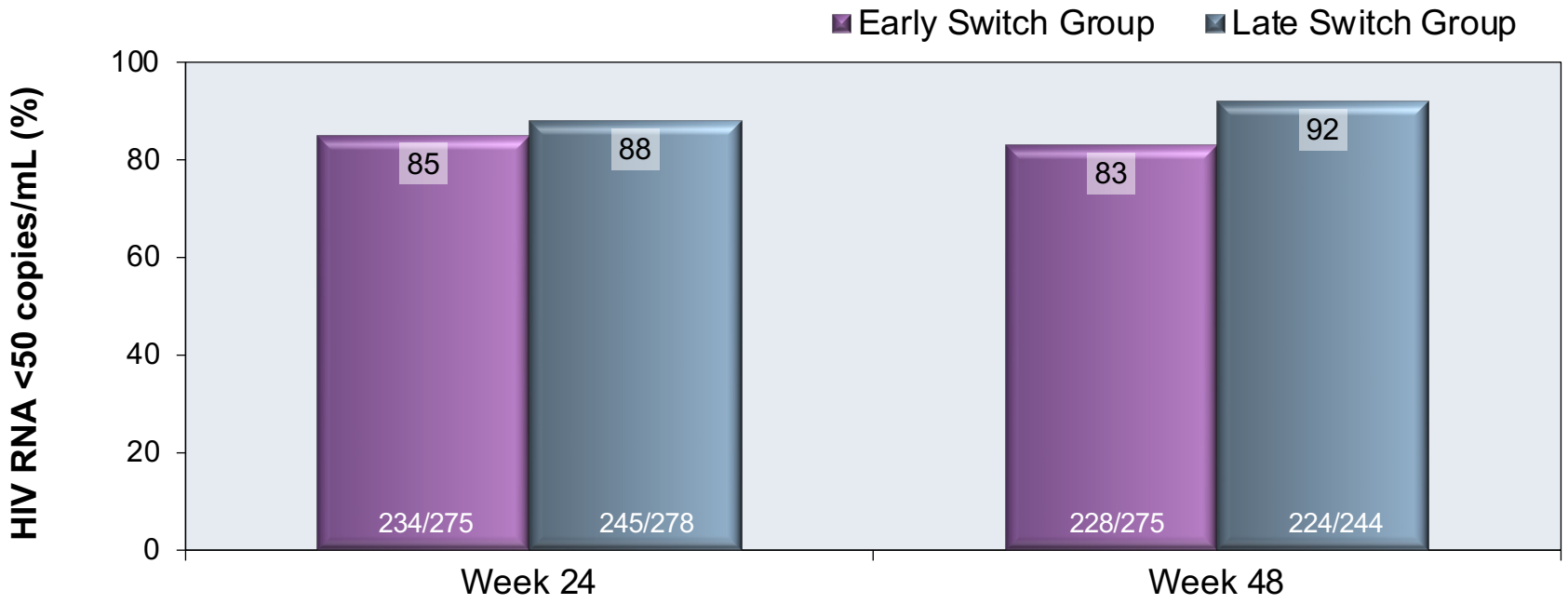


*Baseline antiretroviral therapy (ART) consisting of 2 NRTIs + Anchor drug (NNRTI, PI, or INSTI)

Source: Trottier B, et al. Antivir Ther. 2017;22:295-305.

Switch to Dolutegravir-Abacavir-Lamivudine (DTG-ABC-3TC) STRIIVING: Results

Week 24 and 48 Virologic Response



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Dolutegravir-Abacavir-Lamivudine
Summary of Key Studies

- **Trials in Treatment Naïve Adults**
  - SINGLE[1]: DTG + ABC-3TC versus EFV-TDF-FTC
    - DTG plus ABC-3TC had a better safety profile and higher rates of virologic suppression through 48 weeks than EFV-TDF-FTC
  - GS-380-1489[2]: BIC-TAF-FTC versus DTG-ABC-3TC
    - BIC-TAF-FTC had better tolerability, comparable safety profile and was non-inferior to DTG-ABC-3TC in achieving virological suppression at 48 weeks.
- **Trials In Adults with Virologic Suppression**
  - STRIVIING[3]: Switch to DTG-ABC-3TC or stay on baseline ART
    - DTG-ABC-3TC is safe and efficacious as a potential switch option for the treatment of HIV-1 in adults with viral suppression

Source: [1]Walmsley SL, et al. N Engl J Med. 2013;369;1807-18. [2] Gallant J, et al. Lancet. 2017;390:2063-72. [3]Trottier B, et al. Antivir Ther. 2017;22:295-305.

Dolutegravir-Abacavir-Lamivudine Adverse Effects

- **Hypersensitivity reaction**
  - ABC hypersensitivity: Serious and potentially fatal multi-organ failure and/or anaphylaxis ≤ 6weeks of starting treatment, typically in HLA-B*5701-positive persons
- **Hepatotoxicity**
  - Severe acute exacerbations of HBV in individuals co-infected with HIV and HBV
  - Drug-induced liver injury due to DTG
  - Hepatomegaly and steatosis due to ABC and/or 3TC
- **Lactic Acidosis**
  - Reported with use of NRTIs, including ABC and 3TC
- **Other**
  - Insomnia, headache, hyperglycemia, CPK elevation, increase in serum creatinine

Dolutegravir-Abacavir-Lamivudine
Editor's Summary

- Once daily single-tablet combination regimen with high genetic barrier to resistance
- Well-tolerated regiment, but large pill that may be difficult to swallow
- Do not use in patients with positive HLA-B*5701 test
- Combine with an additional HBV active antiviral agent in patients with HIV-HBV coinfection
- The need for HLA-B*5701 testing prior to use precludes rapid or same-day initiation
- Potential switch option for individuals with viral suppression

Acknowledgments

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