National HIV Curriculum

Dolutegravir-Abacavir-Lamivudine (*Triumeq*)

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Dolutegravir-Abacavir-Lamivudine

Dolutegravir-Abacavir-Lamivudine

50 mg → INSTI

600 mg → NRTI

300 mg → NRTI

Dose: 1 tablet once daily with or without food

Dolutegravir-Abacavir-Lamivudine

- **Indication**
  - Treatment of HIV-1 infection in adults and pediatric patients weighing at least 10 kg
- **Contraindications and precautions**
  - Do not administer if positive for HLA-B*5701 allele (risk of life-threatening hypersensitivity reaction due to abacavir component); always check the HLA-B*5701 test before prescribing
  - Contraindicated with moderate-to-severe hepatic impairment
  - Not adequate treatment for hepatitis B infection
  - Caution if history of ischemic cardiovascular disease or risk factors for ischemic cardiovascular disease (due to the abacavir component)
- **Adverse Events**: (≥2%)
  - Insomnia, headache, fatigue

Source: *Triumeq* FDA prescribing information.

Dolutegravir-Abacavir-Lamivudine
Summary of Key Phase 3 Studies*

- **Trials in Treatment-Naïve Adults**
  - SINGLE: DTG + ABC-3TC versus EFV-TDF-FTC
  - ARIA: DTG-ABC-3TC versus ATV + RTV + TDF-FTC
  - GS-380-1489: DTG-ABC-3TC versus BIC-TAF-FTC
- **Trials in Adults with Virologic Suppression**
  - STRIIVING: DTG-ABC-3TC vs. Continuation of Regimen

*Note: these studies include the three medications dolutegravir (DTG), abacavir (ABC), and lamivudine (3TC), given either as a fixed-dose single pill (DTG-ABC-3TC) or as DTG plus the fixed-dose ABC-3TC.

Abbreviations: DTG-ABC-3TC = dolutegravir-abacavir-lamivudine; EFV-TDF-FTC = efavirenz-tenofovir DF-emtricitabine; ATV = atazanavir; RTV = ritonavir; TDF-FTC = tenofovir DF-emtricitabine; BIC-TAF-FTC = bictegravir-tenofovir alafenamide-emtricitabine

Dolutegravir-Abacavir-Lamivudine

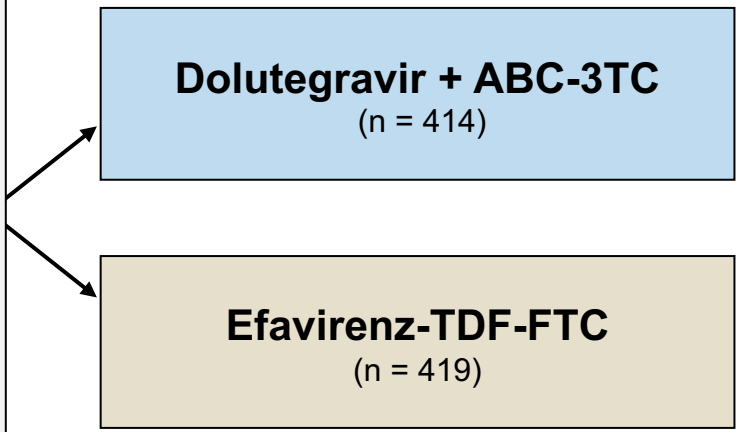
Trials in Treatment Treatment-Naïve Adults

Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC

SINGLE Study

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

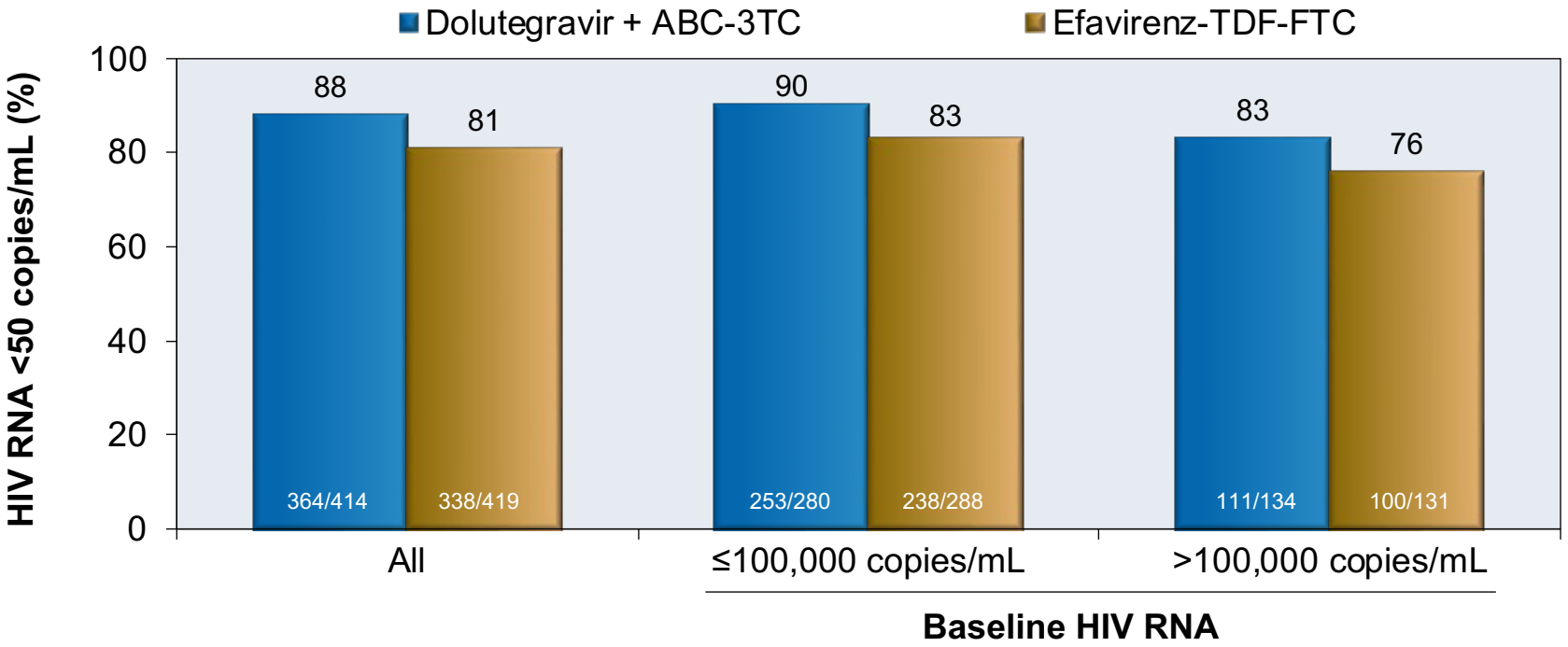
- **Background**:
  - Randomized, double-blind study, phase 3 trial comparing dolutegravir + abacavir-lamivudine with efavirenz-tenofovir DF-emtricitabine
- **Inclusion Criteria (n = 833)**
  - Antiretroviral-naïve adults
  - Age ≥18 years
  - HIV RNA ≥1,000 copies/mL
  - No active CDC AIDS-defining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

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



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

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

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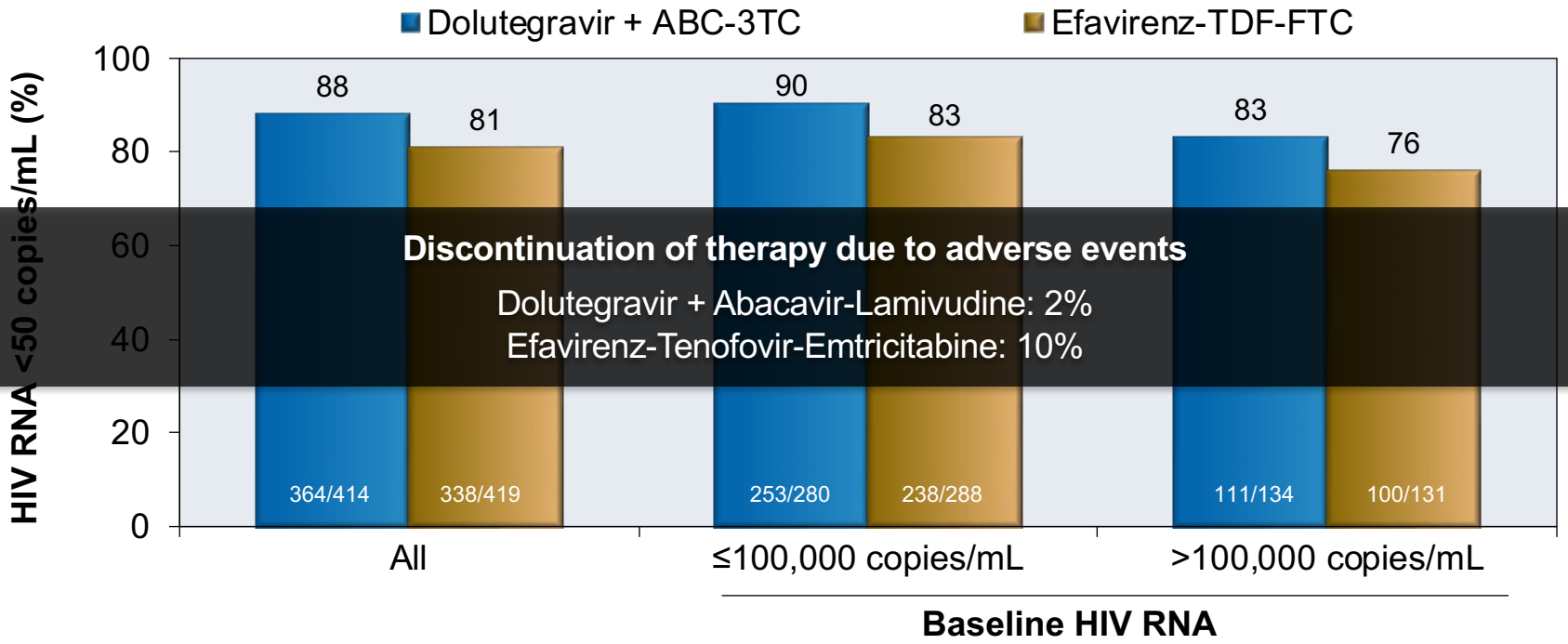
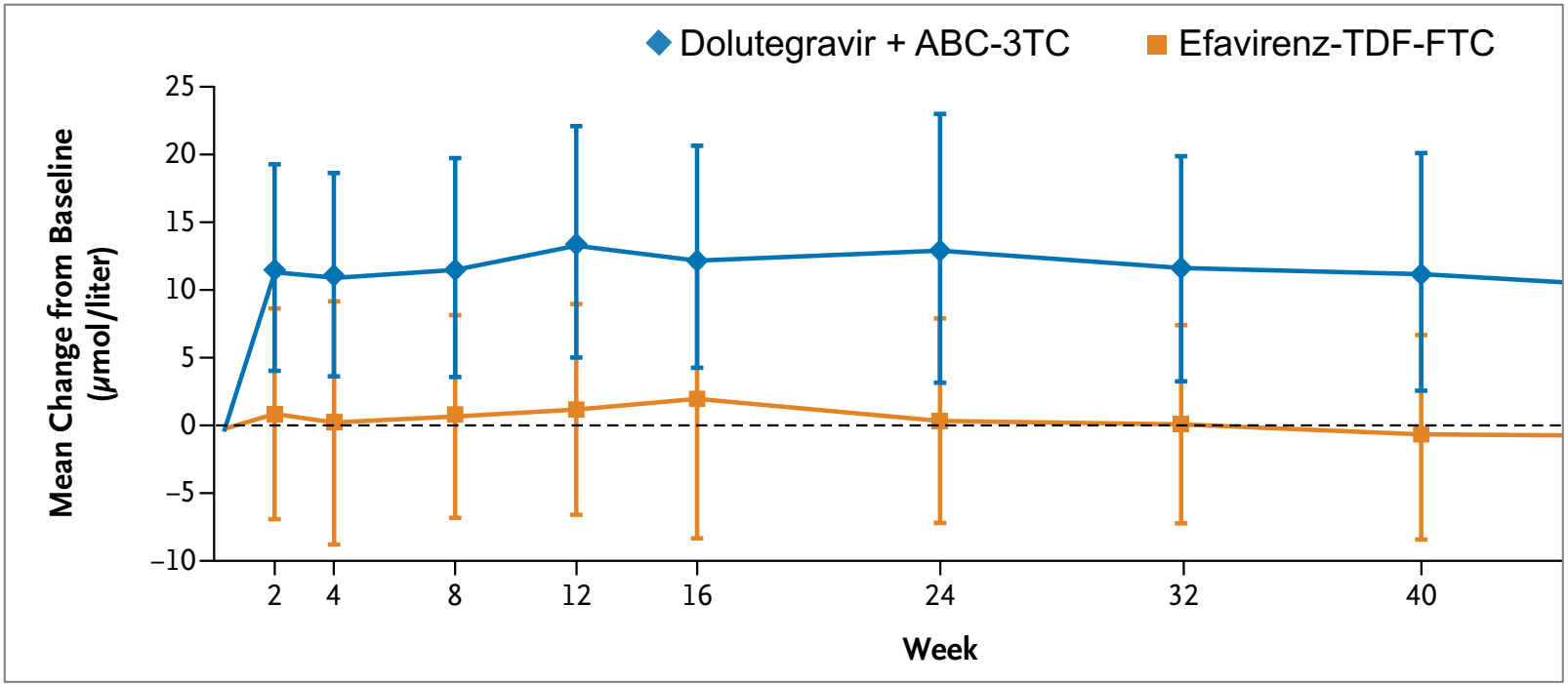


Source: Walmsley SL, et al. N Engl J Med. 2013;369;1807-18.

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

Mean Change from Baseline in Serum Creatinine Levels



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

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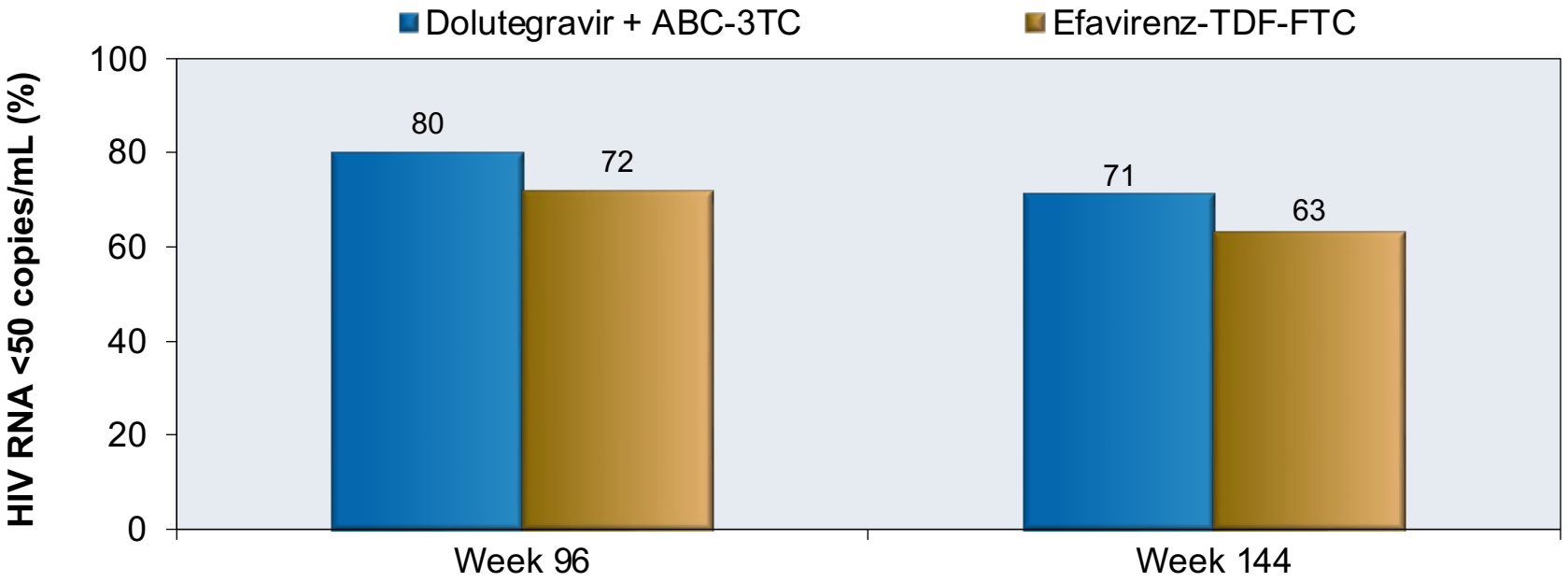
Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC SINGLE Study: Conclusions

Conclusions: “Dolutegravir plus abacavir-lamivudine had a better safety profile and was more effective through 48 weeks than the regimen with 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: Results

Week 96 and Week 144 Virologic Response (Intention-to-Treat Analysis)



Source: Walmsley SL, et al. J Acquir Immune Defic Syndr. 2015;70:515-19.

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

Treatment Emergent Adverse Events (AEs >5%)				
	DTG-ABC-3TC (n = 414)		EFV-TDF-FTC (n = 419)	
	Week 96	Week 144	Week 96	Week 144
Any, %	44	+1	67	+1.2
Dizziness, %	7	+0	33	+0.2
Abnormal dreams, %	7	+0	16	+0.2
Nausea, %	11	+0.2	12	+0
Insomnia, %	10	+0	6	+0.7
Diarrhea, %	6	+0	8	+0
Fatigue, %	7	+0	7	+0
Headache, %	6	+0	7	+0
Rash, %	<1	+0	8	+0

Source: Walmsley SL, et al. J Acquir Immune Defic Syndr. 2015;70:515-19.

DTG-ABC-3TC versus ATV + RTV + TDF-FTC for Treatment-Naïve Women

ARIA

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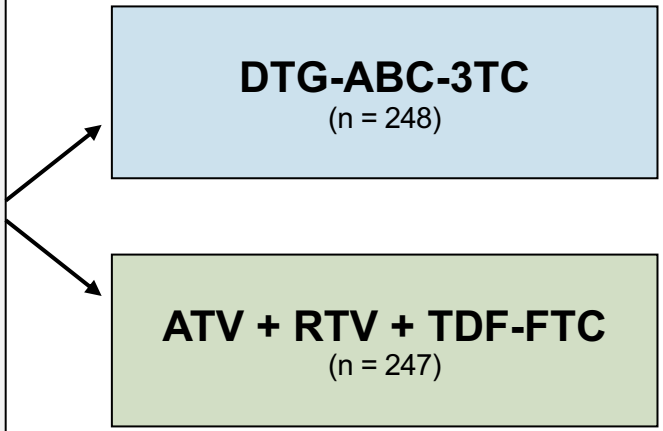
DTG-ABC-3TC vs. ATV +RTV + TDF-FTC for Treatment-Naïve Women
ARIA: Study Design

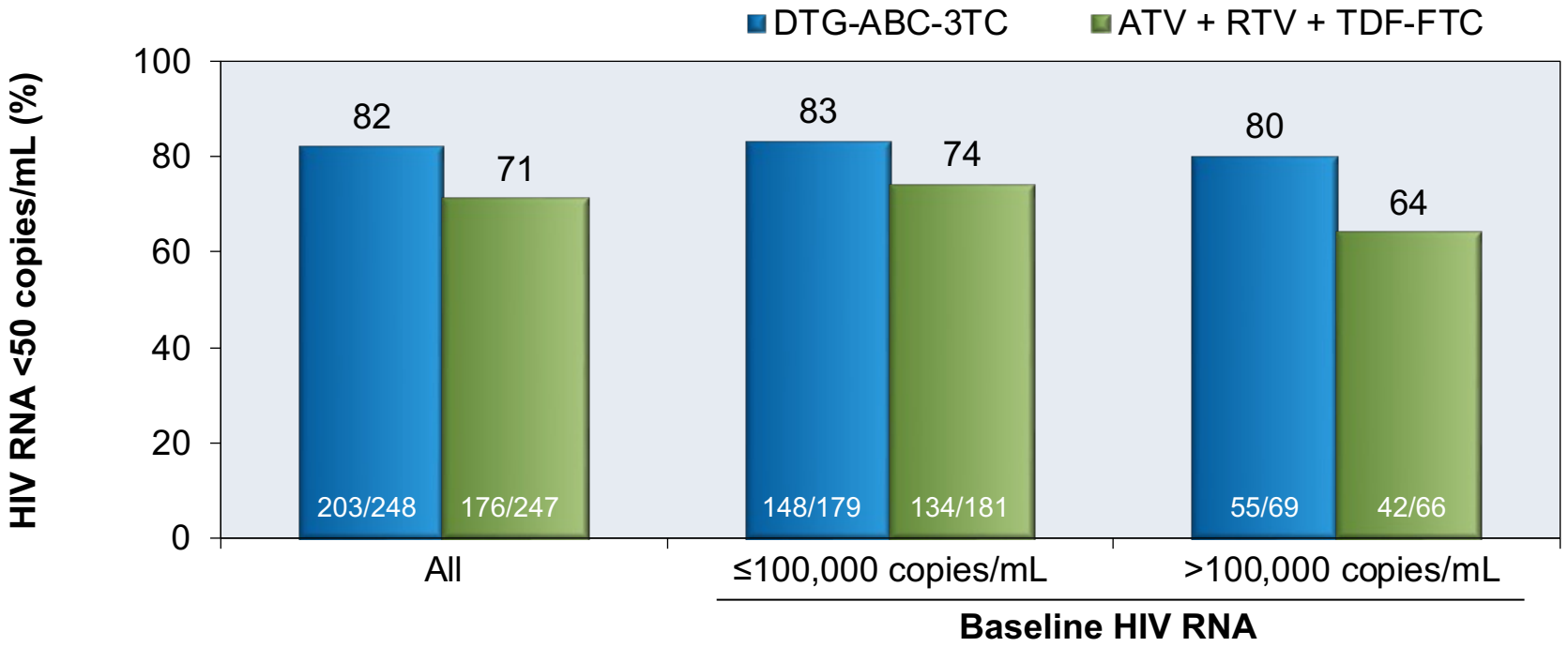
- **Background**: Phase 3b, randomized, open label, multicenter, active controlled, noninferiority trial in women
- **Inclusion Criteria** (n = 495 analyzed)
  - Age ≥18 years and assigned female sex at birth
  - HIV RNA ≥500 copies/mL
  - Received ≤10 days of ART prior to enrollment
  - HLA-B*5701 negative
  - Not pregnant
  - No hepatic impairment
  - Creatinine clearance ≥50 mL/min
  - No resistance to study drugs
- **Treatment Arms** (all meds given once daily)
  - Dolutegravir-abacavir-lamivudine (DTG-ABC-3TC)
  - Atazanavir (ATV) + ritonavir (RTV) + tenofovir DF-emtricitabine (TDF-FTC)



Source: Orrell C, et al. Lancet HIV. 2017;4:e536-46.

DTG-ABC-3TC vs. ATV +RTV + TDF-FTC for Treatment-Naïve Women ARIA: Results

Week 48 Virologic Response, by Baseline HIV RNA Level (Intention-to-Treat Analysis)



Source: Orrell C, et al. Lancet HIV. 2017;4:e536-46.

DTG-ABC-3TC vs. ATV +RTV + TDF-FTC for Treatment-Naïve Women ARIA: Results

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

Snapshot Virologic Outcomes at 48 Weeks		
	DTG-ABC-3TC (n = 248)	**ATV + RTV + TDF-FTC** (n = 247)
Virologic success	82%	71%
Virologic failure	6%	14%
No virologic data	12%	15%

Source: Orrell C, et al. Lancet HIV. 2017;4:e536-46.

DTG-ABC-3TC vs. ATV +RTV + TDF-FTC for Treatment-Naïve Women ARIA: Results

Treatment Emergent Adverse Events (AEs)		
	DTG-ABC-3TC (n = 248)	**ATV + RTV + TDF-FTC** (n = 247)
Any AE	79%	80%
Drug-related AE	33%	49%
Psychiatric AE	14%	14%
Serious AE	5%	8%
Discontinuation due to AE	4%	7%

Source: Orrell C, et al. Lancet HIV. 2017;4:e536-46.

DTG-ABC-3TC vs. ATV +RTV + TDF-FTC for Treatment-Naïve Women ARIA: Results

Treatment Emergent Adverse Events (AEs)		
	DTG-ABC-3TC (n = 248)	**ATV + RTV + TDF-FTC** (n = 247)
Nausea	13%	14%
Diarrhea	5%	7%
Dyspepsia	2%	6%
Ocular icterus	0%	7%
Headache	2%	6%
Jaundice	0%	5%
Insomnia	4%	4%
Depression	2%	3%
Suicidal ideation	2%	1%

Source: Orrell C, et al. Lancet HIV. 2017;4:e536-46.

DTG-ABC-3TC vs. ATV +RTV + TDF-FTC for Treatment-Naïve Women
ARIA: Conclusions

Interpretation: “The non-inferior efficacy and similar safety profile of the dolutegravir combined regimen compared with the atazanavir regimen support the use of dolutegravir for HIV-1 infection in treatment-naive women.”

Source: Orrell C, et al. Lancet HIV. 2017;4:e536-46.

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

GS-380-1489

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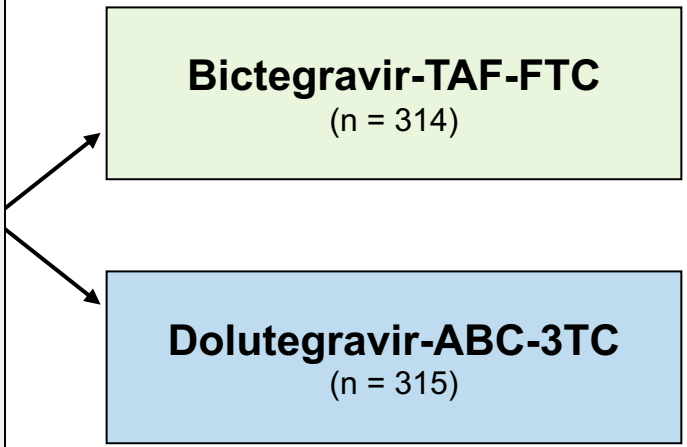
BIC-TAF-FTC versus DTG-ABC-3TC as Initial Therapy
GS-380-1489: Design

- **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

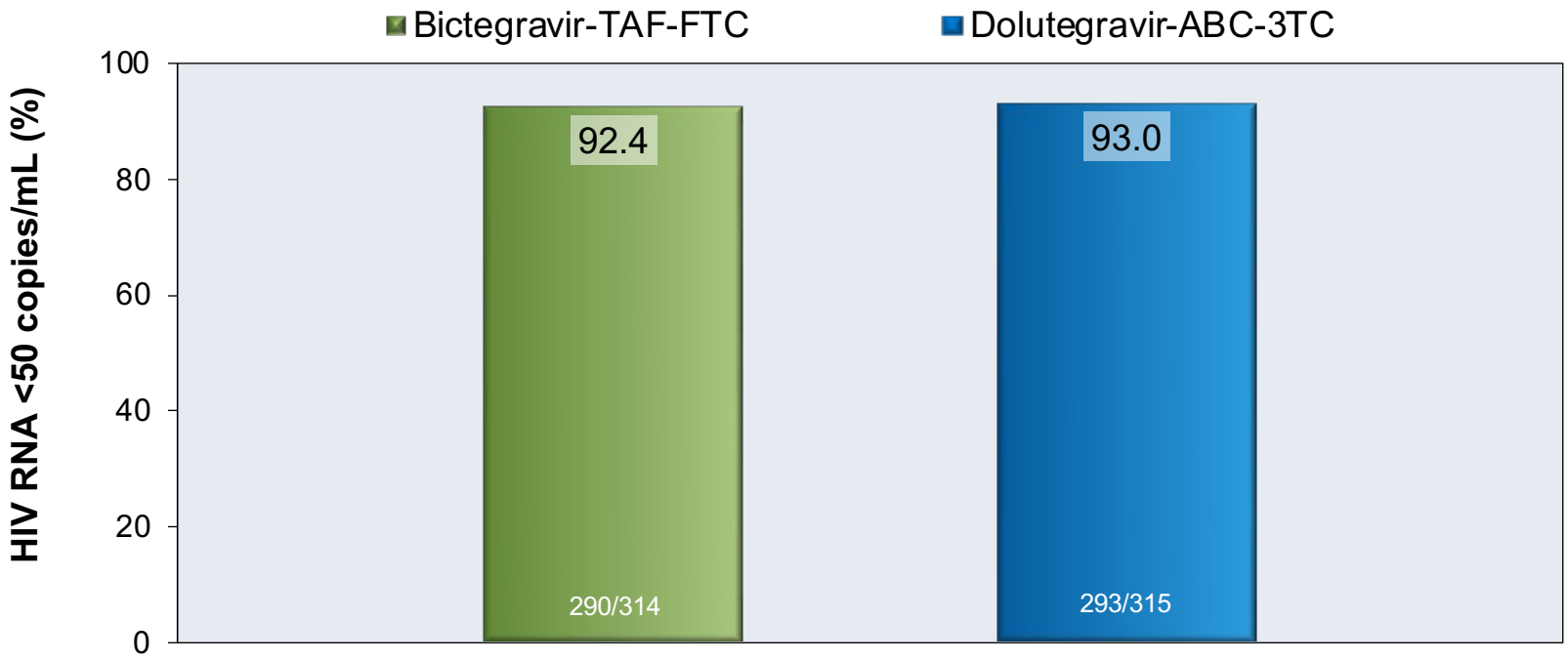
Study GS-380-1489 Baseline Characteristics		
Characteristic	**BIC-TAF-FTC** (n = 314)	**DTG-ABC-3TC** (n = 315)
Median age, years (range)	31 (18-71)	32 (18-68)
Male/Female, %	91/9	90/10
Black or African descent, %	36	36
HIV RNA >100,000 copies/mL, %	17	16
CD4 count <200 cells/mm^3, %	11	10
Median CrCl,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

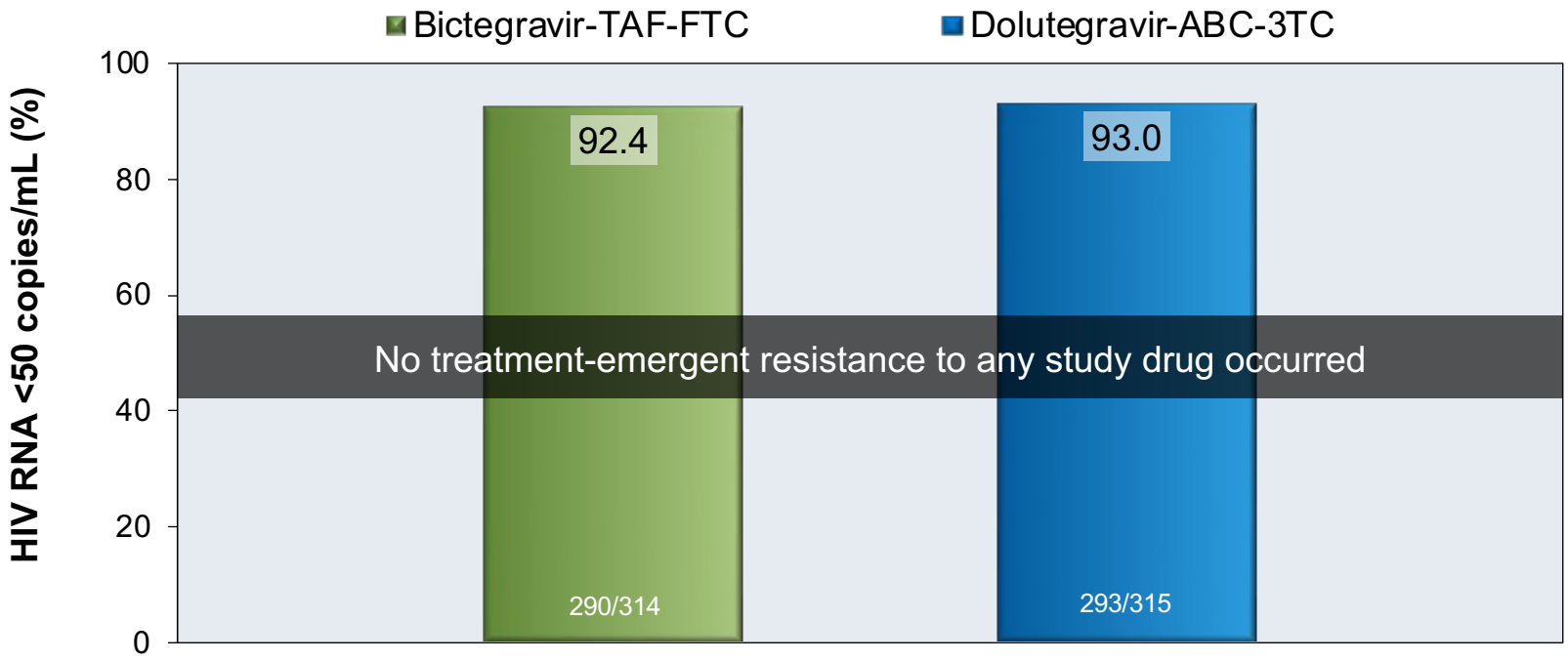
Week 48 Virologic Response (Intention-to-Treat Analysis)



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)



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

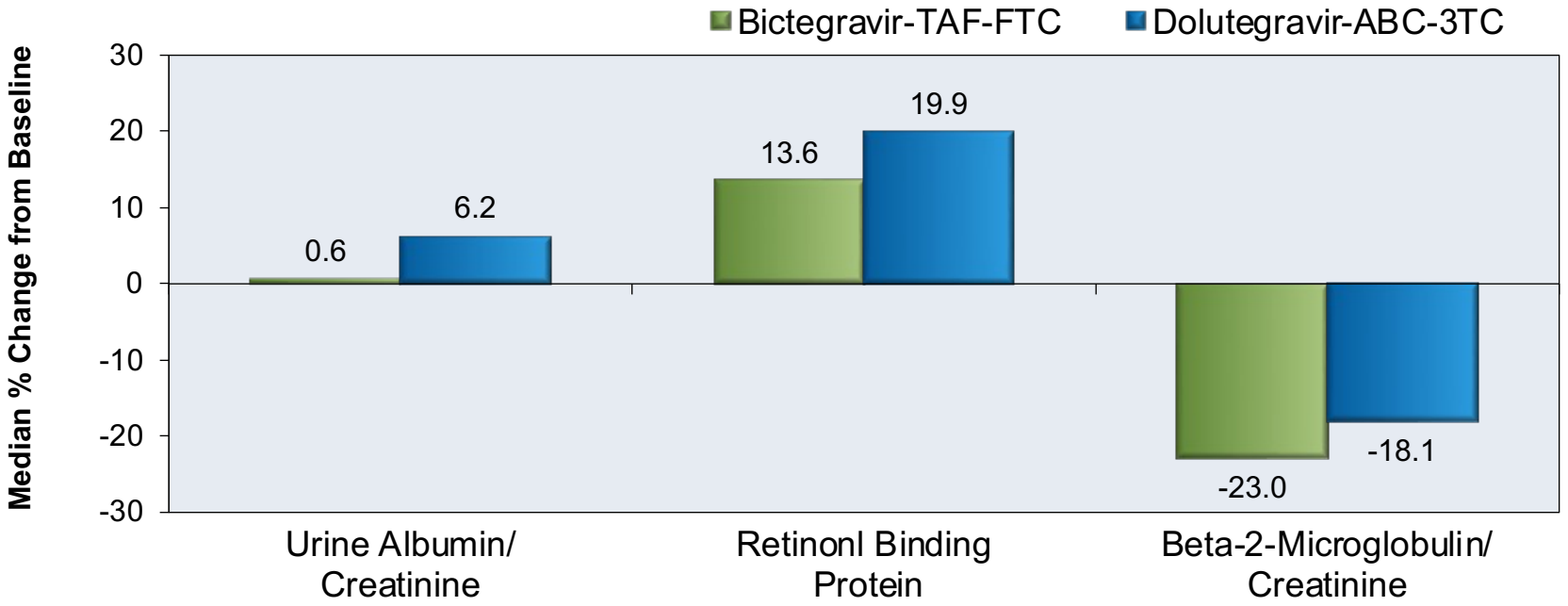
BIC-TAF-FTC versus DTG-ABC-3TC as Initial Therapy
GS-380-1489: Adverse Events

Treatment Emergent Adverse Events (AEs >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

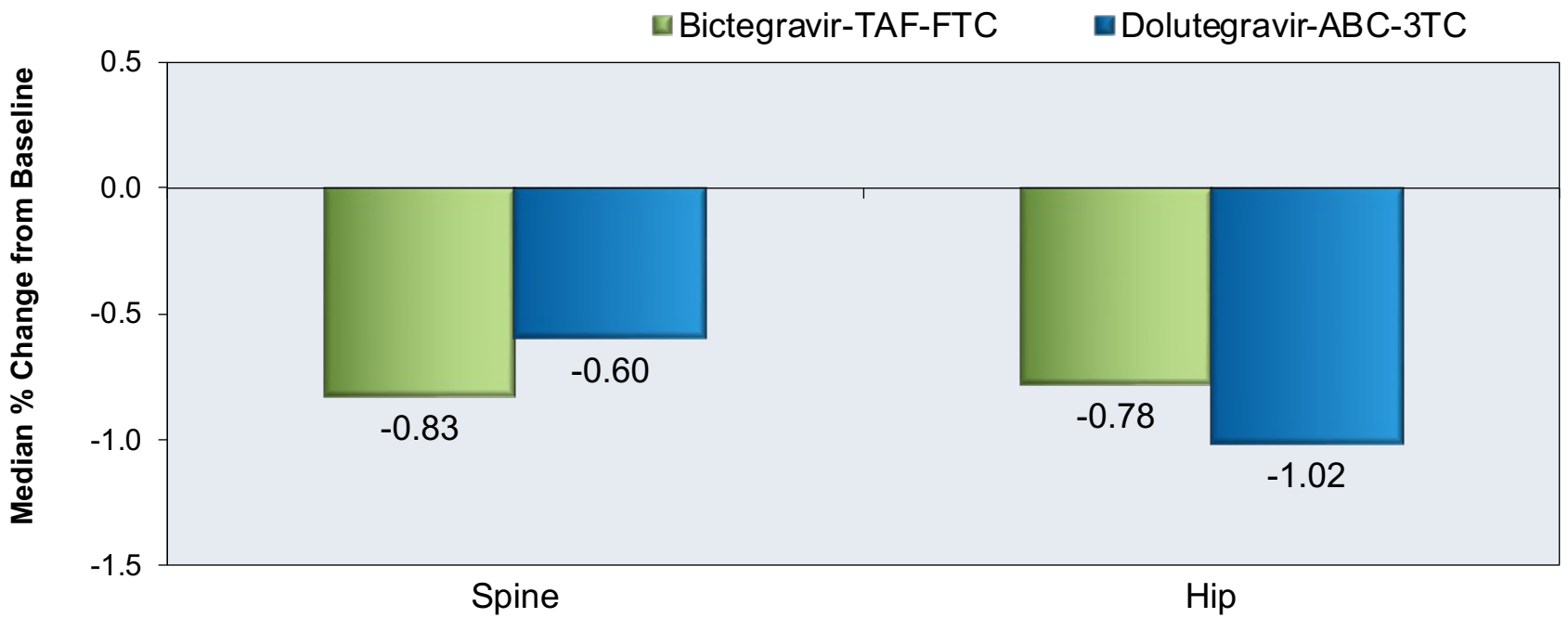
Change in Markers of Proximal Tubulopathy at 48 Weeks



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

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

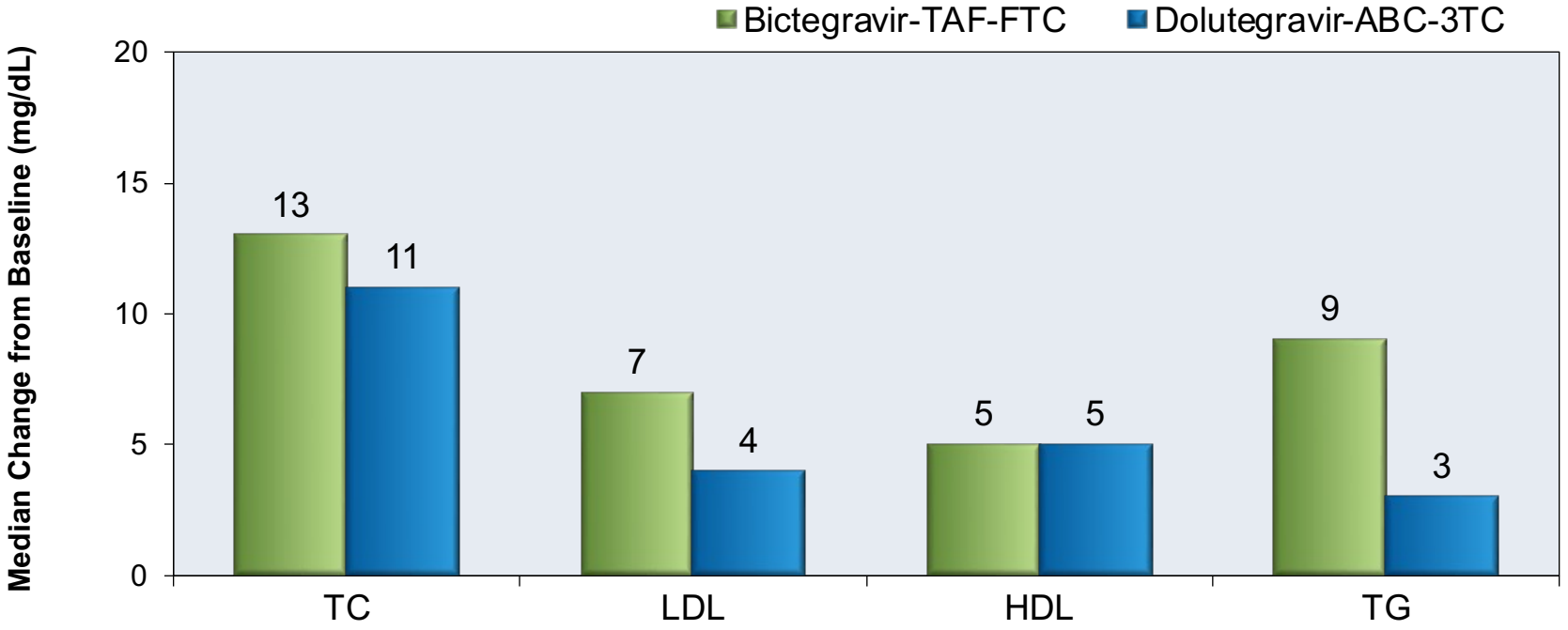
Change in Bone Mineral Density at 48 Weeks



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.

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

Interpretation: “At 48 weeks, coformulated bictegravir, emtricitabine, and tenofovir alafenamide achieved virological suppression in 92% of previously untreated adults and was non-inferior to coformulated dolutegravir, abacavir, and lamivudine, with no treatment-emergent resistance. Bictegravir, emtricitabine, and tenofovir alafenamide was safe and well tolerated with better gastrointestinal tolerability than dolutegravir, abacavir, and lamivudine. Because coformulated bictegravir, emtricitabine, and tenofovir alafenamide does not require HLA B*5701 testing and provides guideline-recommended treatment for individuals co-infected with HIV and hepatitis B, this regimen might lend itself to rapid or same-day initiation of therapy in the clinical setting.”

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

Dolutegravir-Abacavir-Lamivudine

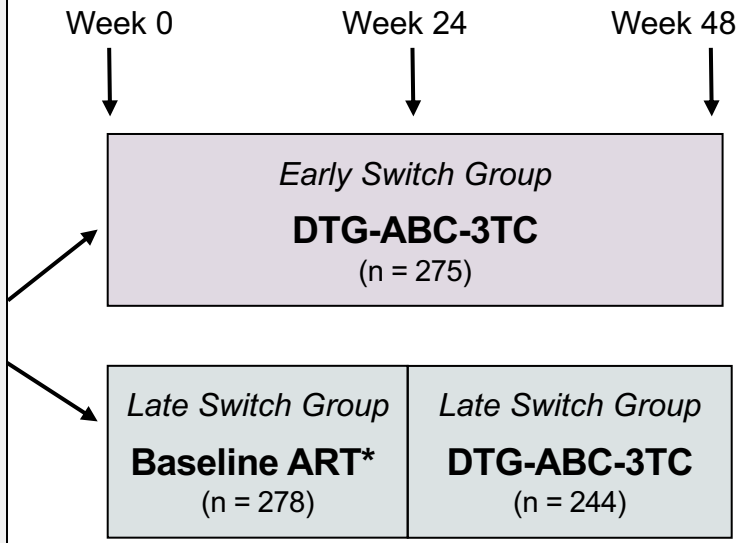
Switch Studies in Adults with Virologic Suppression

Switch to Dolutegravir-Abacavir-Lamivudine

STRIIVING Study

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

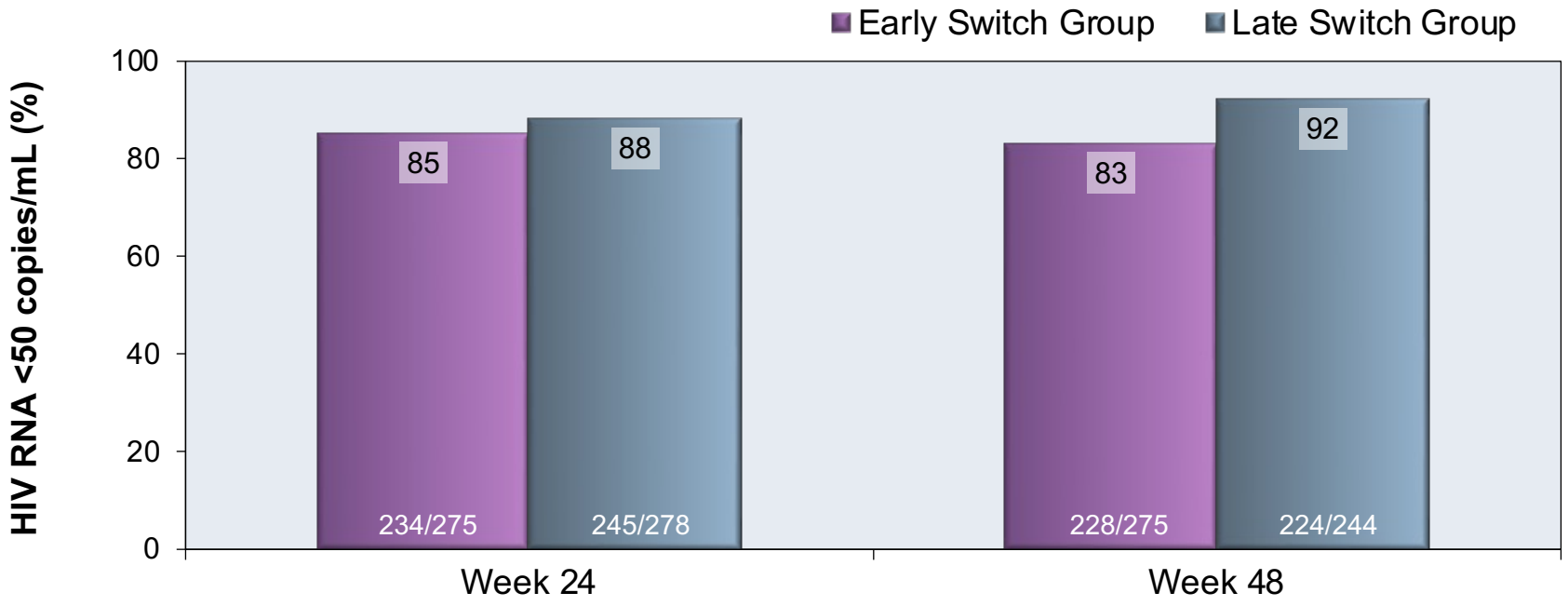


*Baseline antiretroviral therapy (ART): 2 NRTIs + anchor drug (INSTI, NNRTI, or boosted PI)

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



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

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

Conclusions: “Data demonstrating non-inferiority of switching to ABC/DTG/3TC versus continuing current ART support ABC/DTG/3TC as an option when considering switch regimens in HIV-1-infected adults with stable viral suppression.”

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

Acknowledgments

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AETC AIDS Education & Training Center Program

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