AETC AIDS Education & Training Center Program Mountain West

BIKTARVY

Bictegravir-Tenofovir alafenamide-Emtricitabine

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echo

Biktarvy (BIC 50 mg/TAF 25 mg/FTC 200 mg)
FDA approval February 7, 2018

- Outline
  - Clinical trial data
  - FDA approval and indications
  - Drug interactions and drug resistance

See more detail at:
www.hiv.uw.edu
National HIV Curriculum

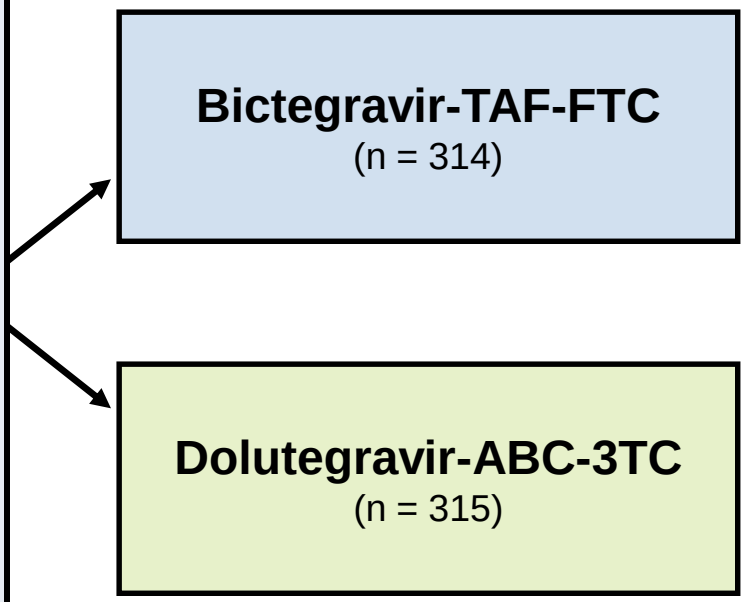
BIC-TAF-FTC vs. DTG-ABC-3TC as Initial Therapy

GS-380-1489

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

GS-1489: Study 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 individuals
- **Inclusion 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
- **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

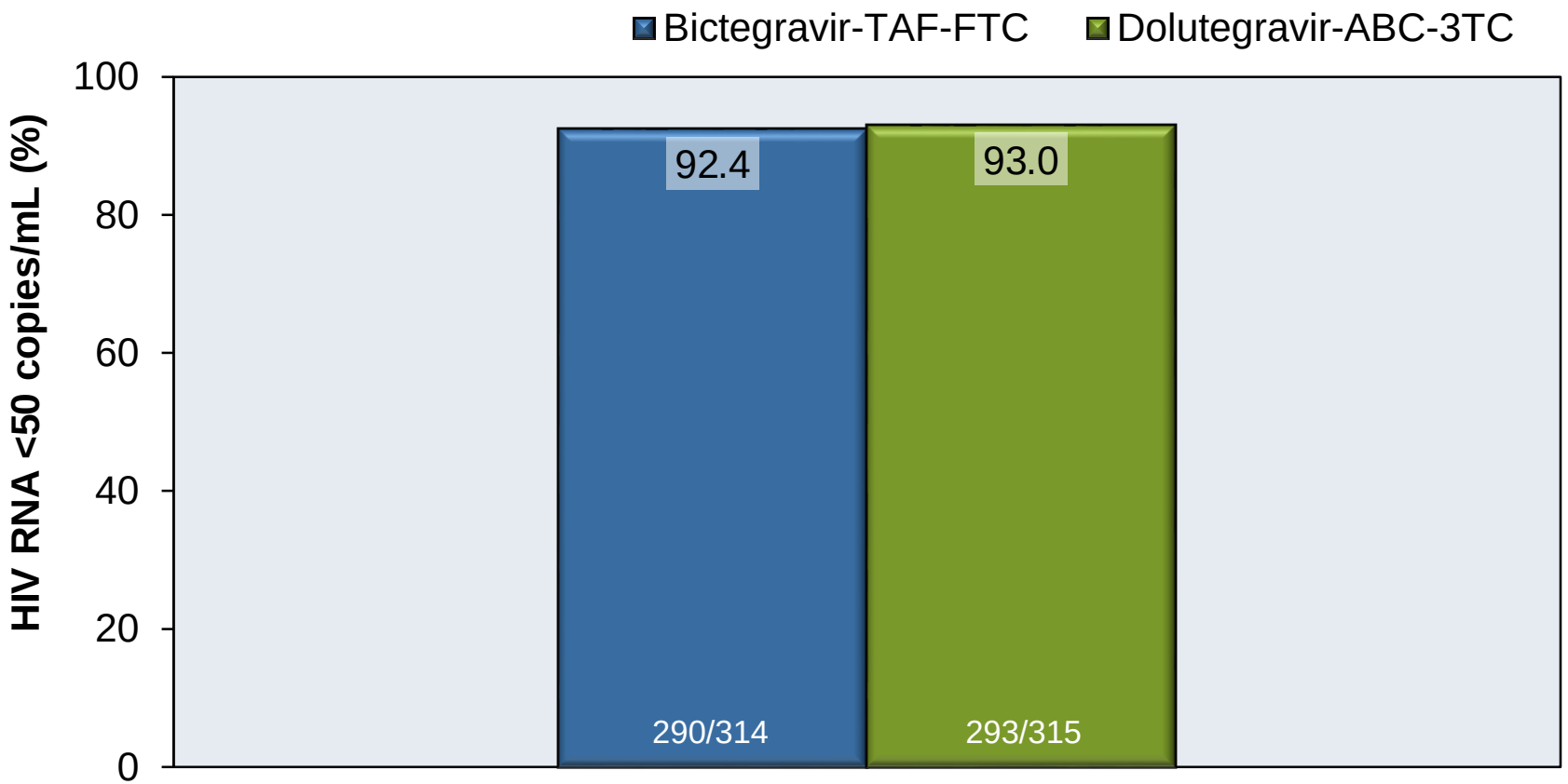
Study 1489 Baseline Characteristics		
Characteristic	**BIC-TAF-FTC (n = 314)**	**DTG + TAF-FTC (n = 315)**
Median age, years (range)	31 (18-71)	32 (18-68)
Male, %	91	90
Black or African descent, %	36	36
HIV RNA >100,000 copies/mL, %	17	16
CD4 count <200 cells/mm^3, %	11	10
Median CrCl, mL/min	125.9	123.0

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)



No treatment-emergent resistance to any study drug occurred

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

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

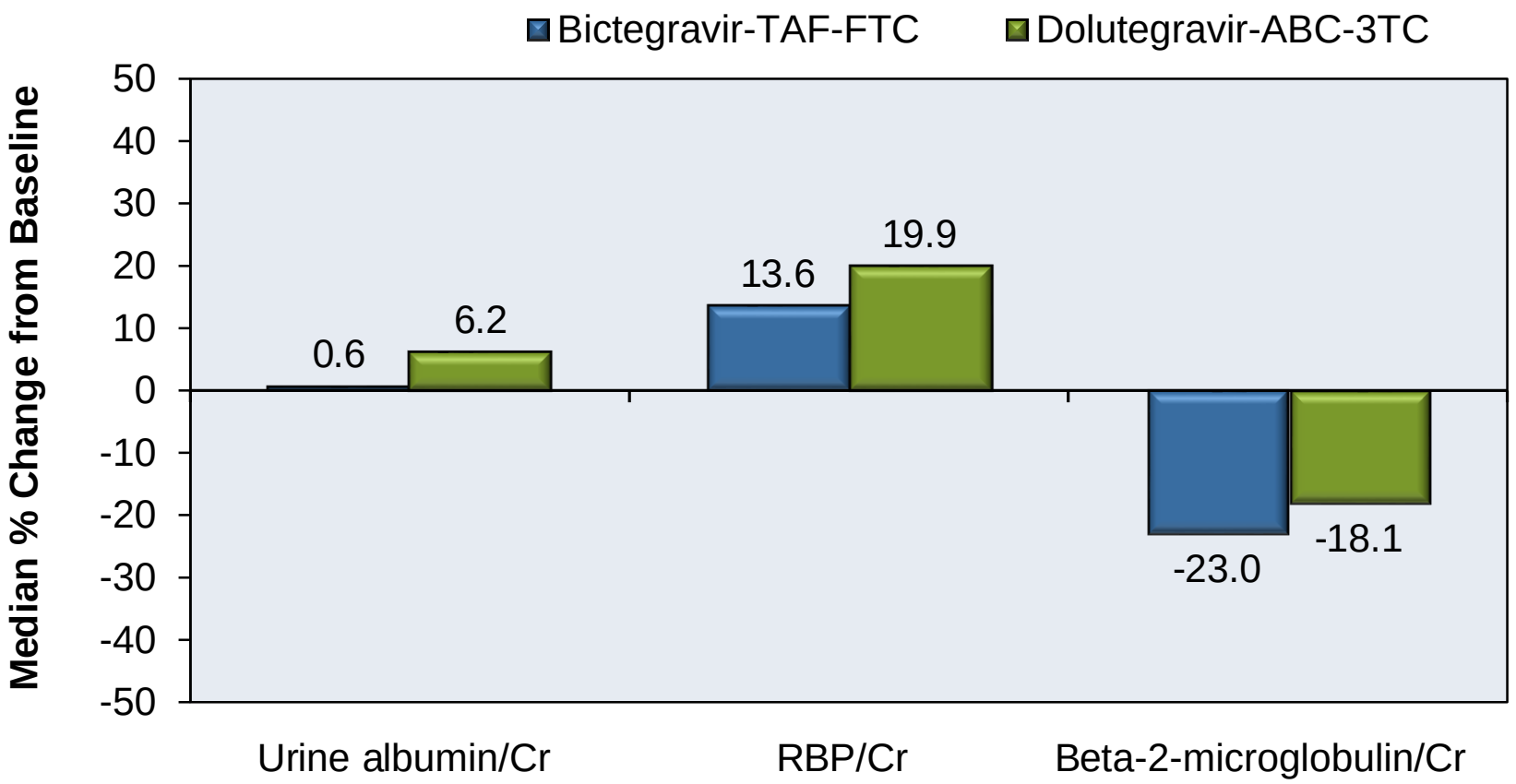
Treatment Emergent Adverse Events in Study 1489 (AE's >5%) Through Week 48		
	BIC-TAF-FTC (n = 314)	**DTG-ABC-3TC** (n = 315)
Diarrhea, %	13	13
Headache, %	11	14
Nausea, %	10	**23**
Fatigue, %	6	9
Arthralgia, %	4	6
Insomnia, %	4	6
Change in eGFR (mL/min)	-10.5	-10.8

Abbreviations: eGFR = estimated glomerular filtration

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

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

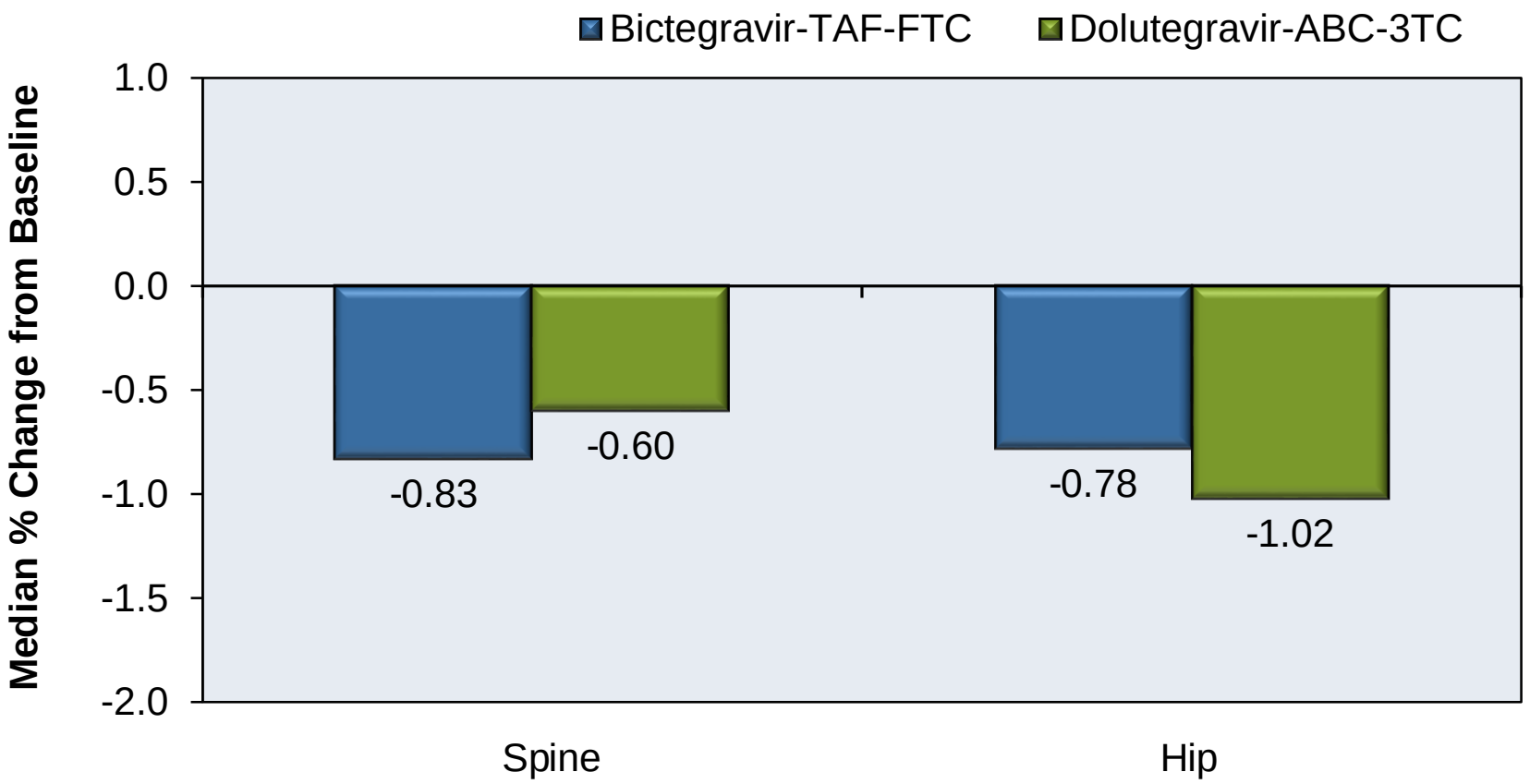
Change in Markers of Proximal Tubulopathy at 48 Weeks



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

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

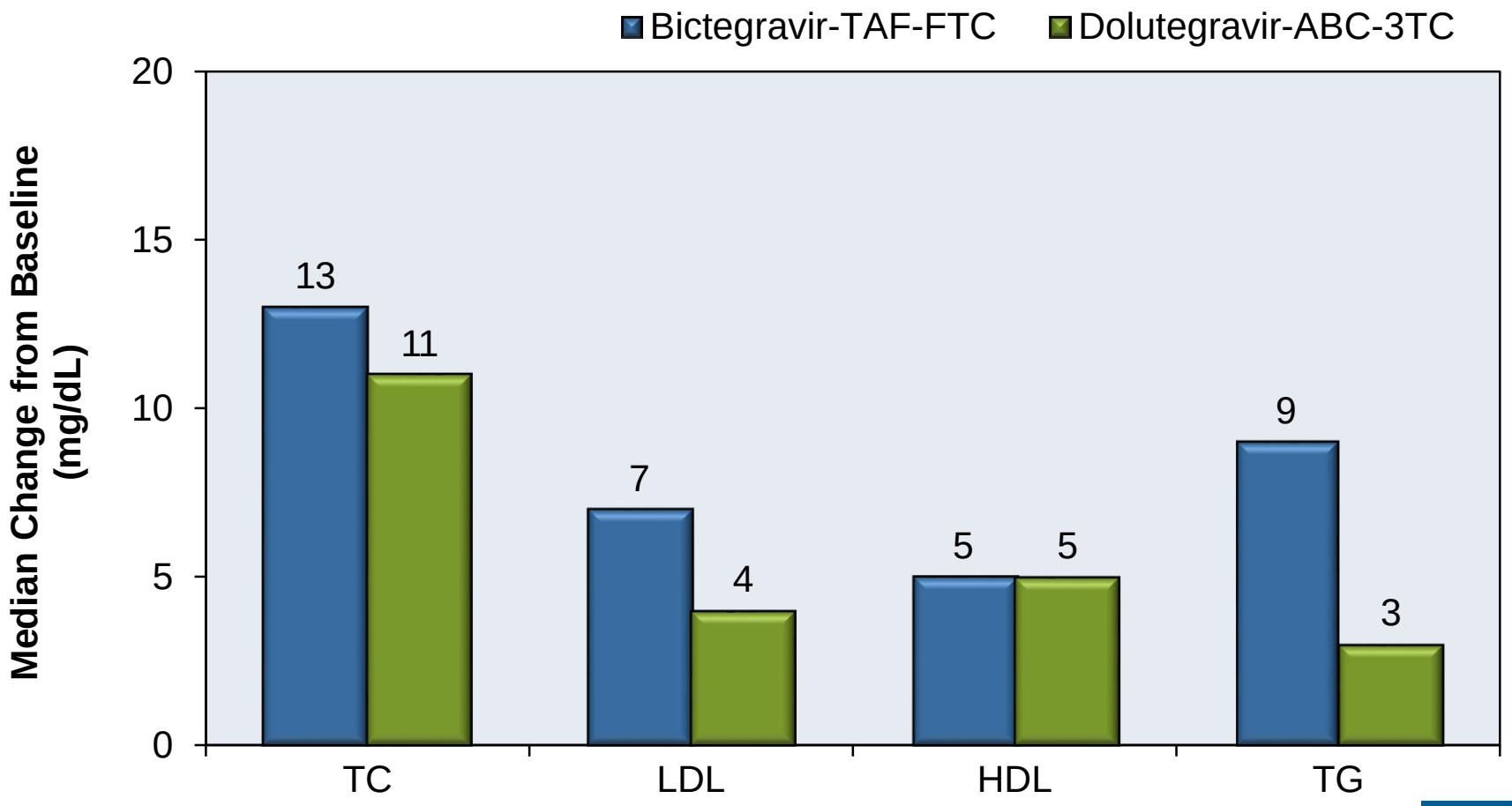
Change in Bone Mineral Density at 48 Weeks



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.

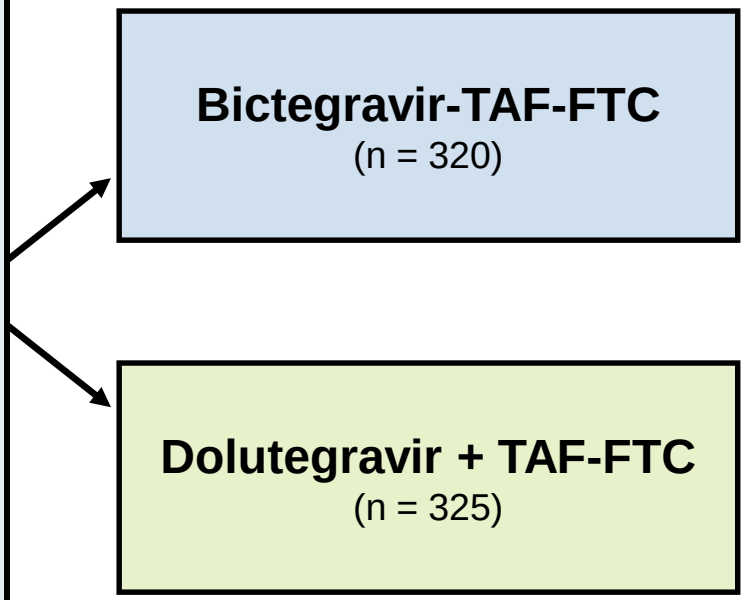
BIC-TAF-FTC vs. DTG + TAF-FTC as Initial Therapy

GS-380-1490

BIC-TAF-FTC vs. DTG + TAF-FTC as Initial Therapy
GS-380-1490: Design

GS-1490: Study Design

- **Background**: Randomized, double-blind, active-controlled, phase 3 study evaluating the efficacy and safety of bictegravir-tenofovir alafenamide-emtricitabine versus dolutegravir plus tenofovir alafenamide-emtricitabine for treatment-naïve individuals
- **Inclusion Criteria**
  - Age ≥18
  - Antiretroviral-naïve (or ≤10 days of treatment)
  - HIV RNA ≥500 copies/mL
  - eGFR ≥30 mL/min
- **Regimens**
  - Bictegravir-TAF-FTC (50/25/200 mg)
  - Dolutegravir (50 mg) + TAF-FTC (200/25 mg)



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

BIC-TAF-FTC vs. DTG + TAF-FTC as Initial Therapy
GS-380-1490: Baseline Characteristics

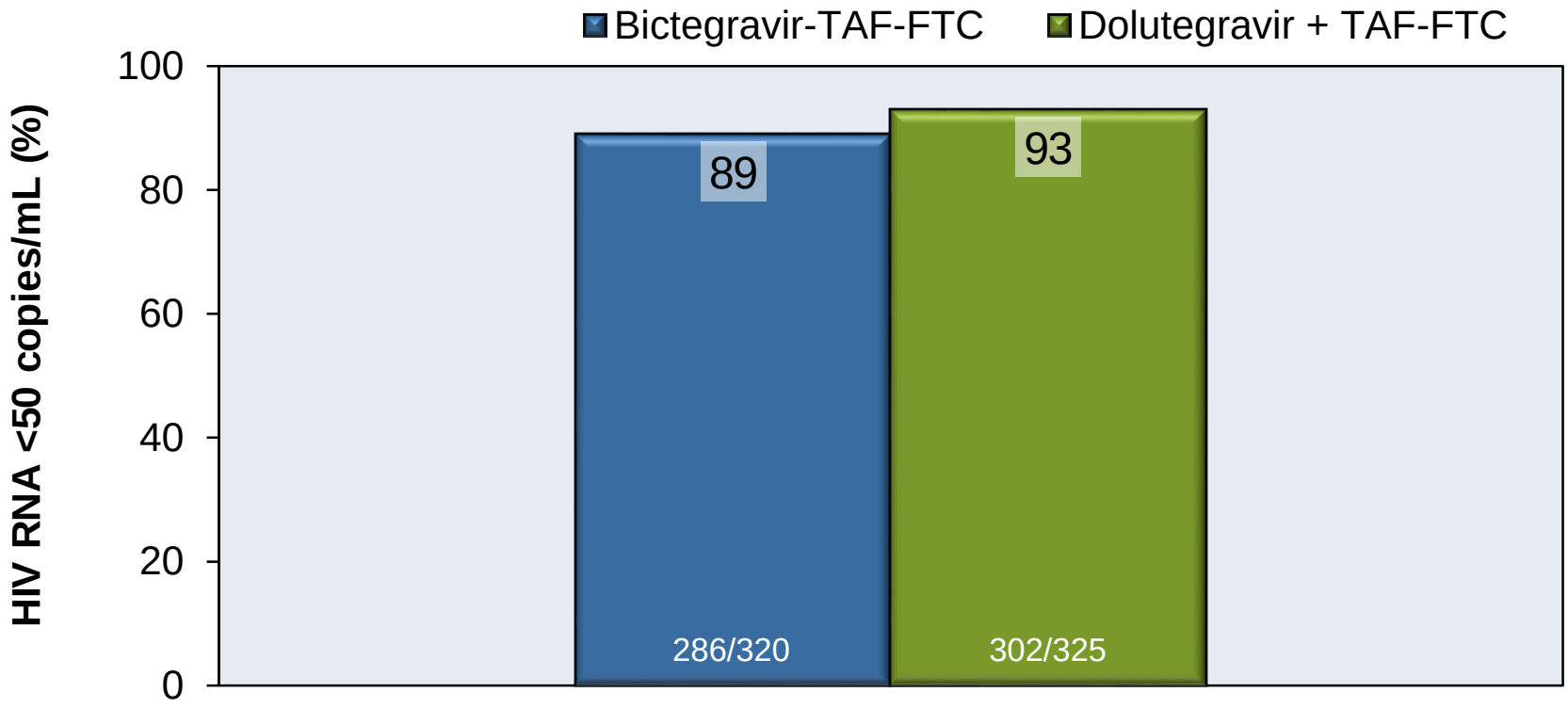
Study 1490 Baseline Characteristics		
Characteristic	**BIC-TAF-FTC (n = 320)**	**DTG + TAF-FTC (n = 325)**
Median age, years (range)	33 (27-46)	34 (27-46)
Male, %	88	89
Black or African descent, %	30	31
HIV RNA >100,000 copies/mL, %	21	17
CD4 count <200 cells/mm^3, %	14	10
HBV coinfection, %	3	2
HCV coinfection, %	2	2
Median CrCl, mL/min	120.4	120.6

Abbreviations: CrCl = creatinine clearance

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

BIC-TAF-FTC vs. DTG + TAF-FTC as Initial Therapy
GS-380-1490: 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.

BIC-TAF-FTC vs. DTG + TAF-FTC as Initial Therapy
GS-380-1490: Results

Treatment Emergent Adverse Events in Study 1490 (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.

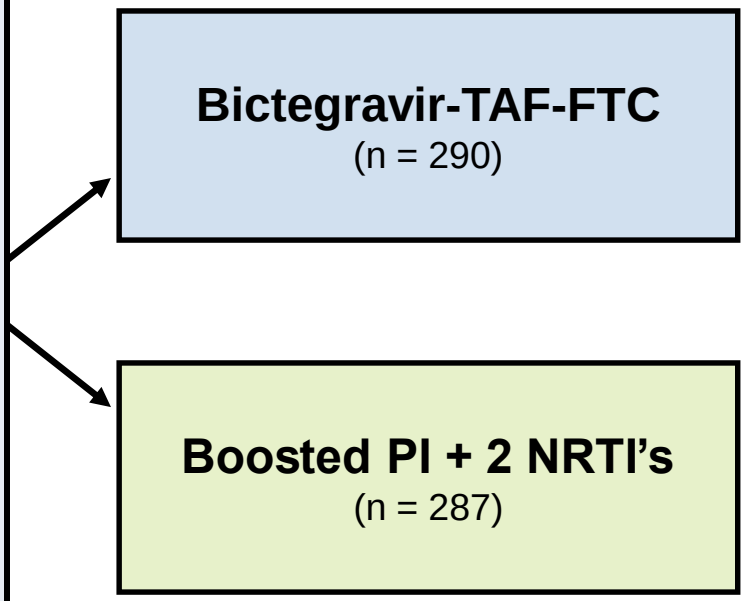
Switch from Boosted PI + 2 NRTI's to BIC-TAF-FTC in Virally Suppressed Adults

GS-380-1878

Switch from Boosted PI to BIC-TAF-FTC
GS-380-1878: Design

GS-1878: Study Design

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



Source: Daar E, et al. ID Week Conference, San Diego, Oct 2017. Abstract LB-4.

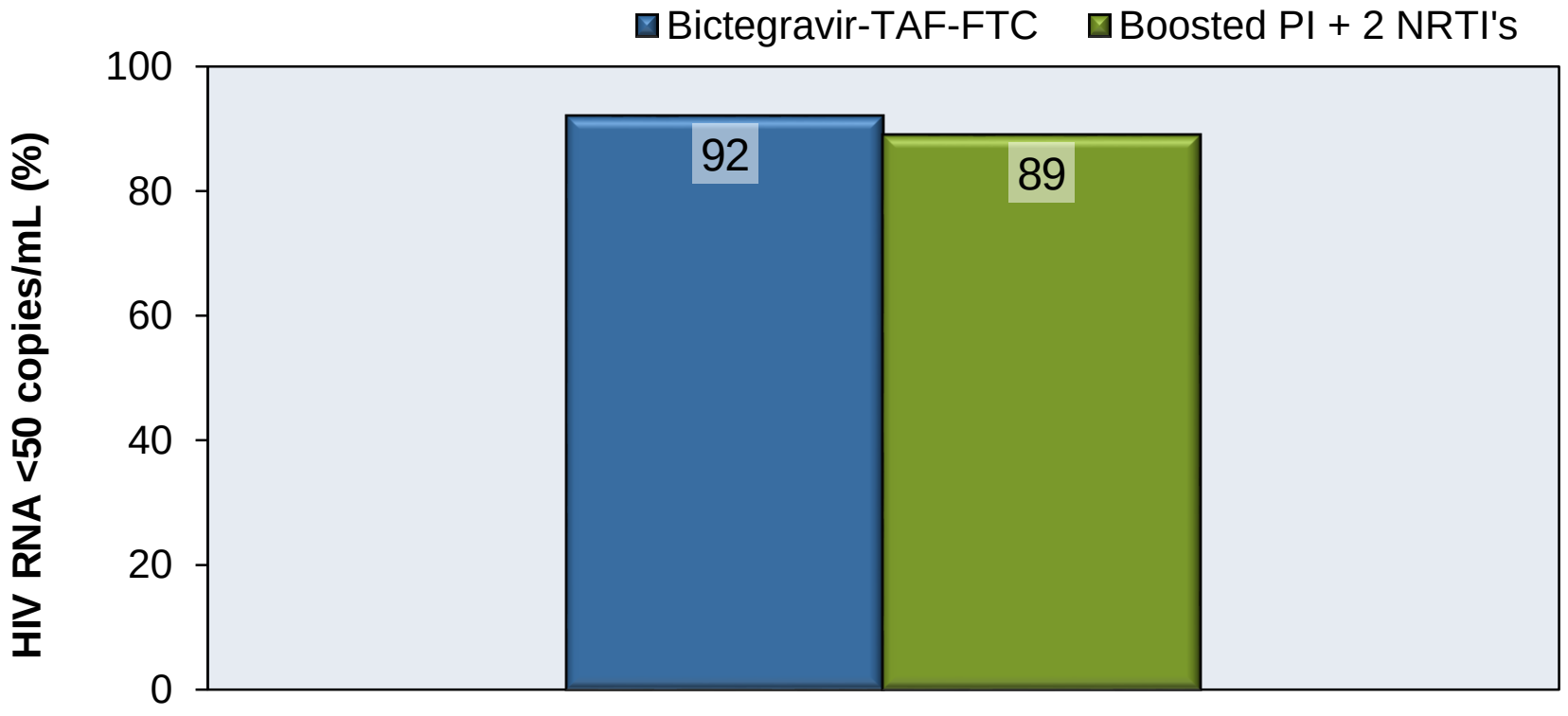
Switch from Boosted PI to BIC-TAF-FTC
GS-380-1878: Baseline Characteristics

Study 1878 Baseline Characteristics		
Characteristic	**BIC-TAF-FTC** (n = 290)	**Boosted PI + 2 NRTI's** (n = 287)
Median age, years (range)	48	47
Male, %	84	82
Black or African descent, %	27	25
Hispanic/Latino, %	21	16
Median CD4, cells/mL	617	626
HBV coinfection, %	8	6
HCV coinfection, %	5	5
Median eGFR, mL/min	107	105
Baseline TDF/FTC, ABC/3TC, %	84, 16	85, 15
Baseline DRV, ATV, %	57, 43	54, 46

Source: Daar E, et al. ID Week Conference, San Diego, Oct 2017. Abstract LB-4.

Switch from Boosted PI to BIC-TAF-FTC
GS-380-1878: Results

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



No treatment-emergent resistance occurred in BIC-TAF-FTC arm
One participant receiving DRV + RTV + ABC-3TC developed L74V
Incidence of grade 3 or 4 AE's similar (4% BIC-TAF-FTC, 6% boosted PI)

Source: Daar E, et al. ID Week Conference, San Diego, Oct 2017. Abstract LB-4.

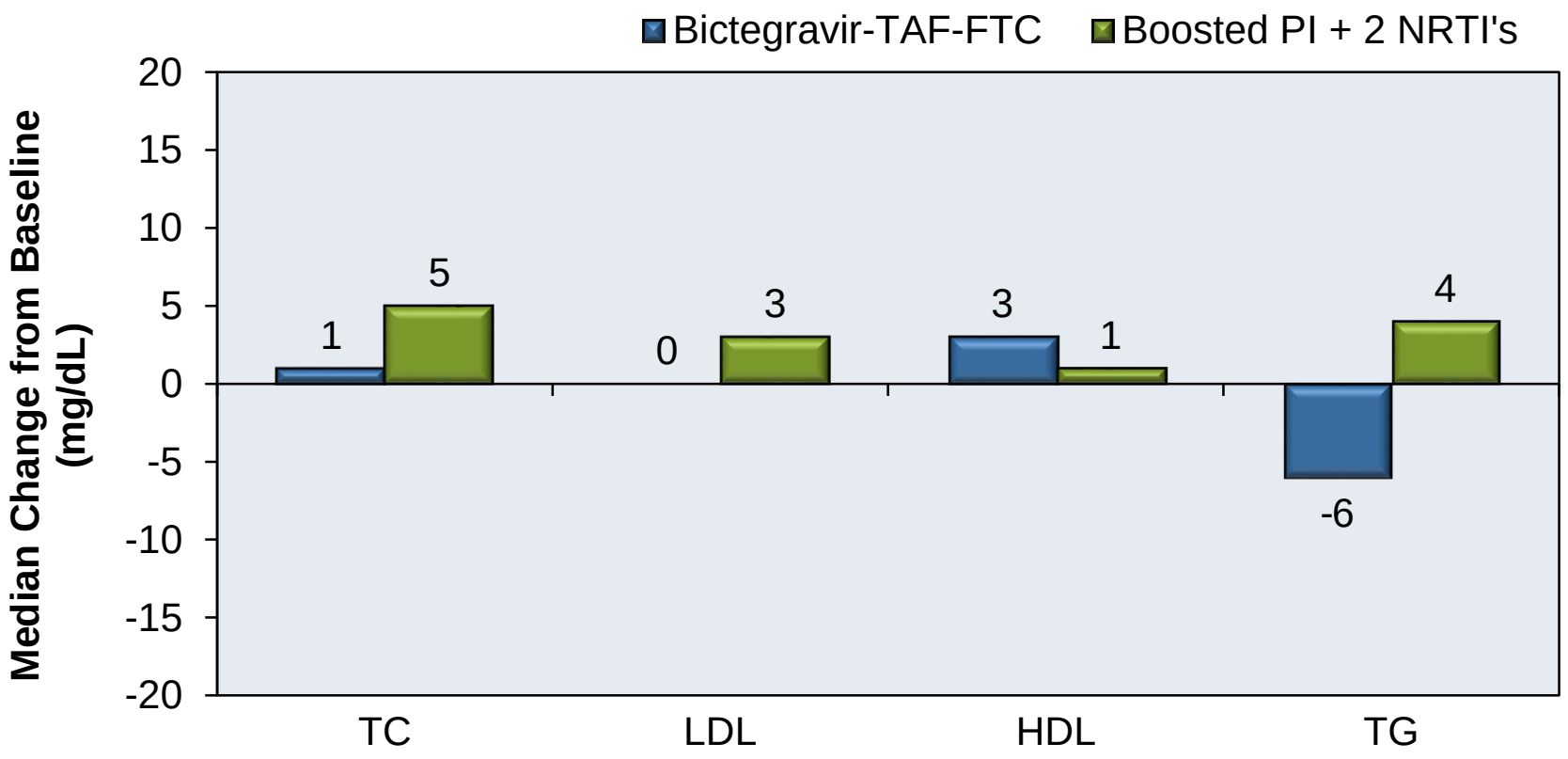
Switch from Boosted PI to BIC-TAF-FTC
GS-380-1878: Results

Treatment Emergent Adverse Events in Study 1878 Through Week 48		
	BIC-TAF-FTC (n = 290)	**Boosted PI + 2 NRTI's** (n = 287)
Headache, %	12	4
Diarrhea, %	8	8
Nasopharyngitis, %	7	12
URI, %	7	8
Back pain, %	5	6
Arthralgia, %	4	5
Change in eGFR	-4.3 mL/min	0.2 mL/min
Abbreviations: eGFR = estimated glomerular filtration		

Source: Daar E, et al. ID Week Conference, San Diego, Oct 2017. Abstract LB-4.

Switch from Boosted PI to BIC-TAF-FTC
GS-380-1878: Results

Change in Lipids at 48 Weeks



Source: Daar E, et al. ID Week Conference, San Diego, Oct 2017. Abstract LB-4

BIC-TAF-FTC (*Biktarvy*)
Indications

- BIKTARVY is indicated as a complete regimen for the treatment of HIV-1 infection in:

  1) Adults who have no ARV treatment history

  2) To replace the current ARV regimen if: virologically suppressed on a stable regimen for ≥3 months with no history of treatment failure and no known resistance to the individual components

Source: Biktarvy package insert, Gilead Sciences.

BIC-TAF-FTC (*Biktarvy*)
Drug Interactions

- Interaction with cations? Yes
  - Take *Bictarvy* fasting 2 hours before antacids containing Al/Mg/Ca[1]
  - Take *Bictarvy* with food simultaneously with Ca/Fe supplements[1]
- Interaction with metformin? Yes, less than DTG
  - BIC → increased metformin AUC 27%-39% and Cmax 27%[2,3]
  - DTG → increased metformin AUC 79% and Cmax 66%[4]
- Interaction with rifampin? Yes, contraindicated[1]

1. Biktarvy package insert. 2. Zhang H et al. 18th Workshop on Clinical Pharmacology of ART, Chicago 2017. 3. Custodio J et al. ID Week, 2017. 4. Song IH et al. JAIDS, Aug 2016.

Bictegravir
Drug Resistance

- Like DTG, in clinical trials development of INSTI or NRTI resistance did not occur with BIC-TAF-FTC failures
  - n=8 evaluated in treatment-naïve trials, 3 in switch trials
- BIC tested against 64 clinical isolates with INSTI mutations
  - Isolates with single mutations E92Q, T97A, Y143C/R, Q148R, or N155H had <2-fold reduced susceptibility
  - Those with >2.5-fold reduced susceptibility had complex patterns (Q148/H/R/K + G140A/C/S +/- other secondary)

Source: BIKTARVY prescribing information. Gilead Sciences.

BIC/TAF/FTC (*Biktarvy*)
Conclusions and Future Directions

- Conclusions:
  - BIC/TAF/FTC is effective for initial or maintenance ART
- Switch trials in virologically suppressed adults:
  - DTG/ABC/3TC or DTG + ABC/3TC (GS-1844)
  - E/C/F/TAF or TDF-containing ART in persons >65 (GS-4449)
  - E/C/F/TDF or E/C/F/TAF or ATV/r + TDF/FTC in women (GS-1961)

Source: clinicaltrials.gov