Update on Options for HIV Prevention and Treatment

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Update on Options for HIV Prevention and Treatment

Update on Options for HIV Treatment (20 min)

Weerawat Manosuthi, MD

Update on Options for HIV Prevention (20 min)

Prof. Sasisopin Kiertiburanakul, MD

Outline

Update on Options for HIV Treatment

HIV Treatment Recommendations and ART Considerations

Clinical Data of BIC/FTC/TAF* on Treatment-naïve Patients

Clinical Data of BIC/FTC/TAF on Treatment-experienced Patients

*Bictegravir, Emtricitabine, and Tenofovir Alafenamide

A 35-year-old MSM with Newly Diagnosed HIV Infection

- A 35-year-old MSM with newly diagnosed HIV infection
  - He reported multiple sexual partners over the past 1 year.
  - He discontinued use of FTC/TDF PrEP 2 years ago.
- His CD4 was 588 cells/mm3. HBsAg was positive and anti-HCV was negative.
- CBC, kidney and liver function test were unremarkable.
- He preferred a single-tablet regimen.

Q: What ARV regimen would you prescribe for this patient? Any consideration?

1. BIC/FTC/TAF
2. DTG/3TC/ABC
3. EFV/FTC/TDF
4. TLD
5. Others

Factors to Consider When Selecting an Initial Regimen

Initial Characteristics to Consider in All Patients

- Pretreatment HIV RNA level
- Pretreatment CD4+ cell count
- HIV genotypic drug resistance testing results
- HLA-B*5701 status
- Patient preferences
- Anticipated adherence to regimen

Specific Comorbidities or Other Conditions

- Cardiovascular disease, hyperlipidemia, renal disease, osteopenia/osteoporosis or conditions associated with BMD loss
- Psychiatric illness, neurologic disease, or drug abuse or dependency requiring narcotic replacement therapy
- Pregnancy or pregnancy potential
- Certain coinfections (i.e. hepatitis C, hepatitis B, tuberculosis)

Regimen-Specific Considerations

- Regimen's genetic barrier to resistance
- Potential adverse drug effects
- Known or potential drug interactions with other medications
- Convenience (i.e. pill burden, dosing frequency, availability of fixed-dose combination products, food requirements)
- Cost

1. US Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf Accessed February 23, 2022.

International Guidance on First-line ART

DHHS[1]	IAS-USA[2]	EACS[3]
Recommended initial regimens for most PWH ▪ BIC/TAF/FTC ▪ DTG/ABC/3TC* ▪ DTG + XTC + TXF ▪ DTG/3TC†	*Generally recommended initial regimens* ▪ BIC/TAF/FTC ▪ DTG + TXF/FTC ▪ DTG + 3TC/TDF ▪ DTG/3TC† ‡	*Recommended regimens* ▪ BIC/FTC/TAF ▪ DTG/ABC/3TC or DTG + ABC/3TC* ▪ DTG + XTC/TXF ▪ RAL + XTC + TXF ▪ DTG/3TC or DTG + 3TC† ▪ DOR/3TC/TDF or DOR+ TAF/FTC or TDF/XTC

*if HLA-B*5701 negative

†Except for individuals with baseline HIV RNA >500,000 cps/mL, with HBV, or for whom results of HIV genotypic resistance testing or HBV testing are not yet available.

‡Possibly not suitable for individuals with baseline CD4 cell count <200 cells/mm^3.

1. DHHS Guidelines. June 2021. 2. Saag MS, et al. JAMA 2020;324:1651-69. 3. EACS Guidelines. October 2021

DHHS Antiretroviral Regimen Options for Treatment-Naïve Patients

4 Recommended Options for "Most People with HIV"

- INSTI plus 2NRTIs: 3 regimens
- INSTI plus 1NRTIs: 1 regimen

3 Recommended Options in "Certain Clinical Situations"

- INSTI plus 2NRTIs: 2 regimens
- Boosted PI plus 2NRTIs: 3 regimens

(boosted DRV is preferred over boosted ATV)

- *DRV/c or DRV/r plus TXF plus XTC*
- *ATV/c or ATV/r plus TXF plus XTC*
- *DRV/c or DRV/r plus ABC/3TC*

- NNRTI plus 2NRTIs: 3 regimens

1. US Department of Health and Human Services. *Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents*. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf Accessed February 23, 2022.

การติดเชื้อเอชไอวี ประเทศไทย ปี 2564/2565

Thailand National Guidelines on HIV/AIDS Treatment and Prevention 2021/2022

http://www.thaiaidssociety.org/index.php?option=com_content&view=article&id=79&Itemid=86

Choosing Among Integrase Inhibitors for First-line ART

Agent[1,2]	Advantages	Disadvantages
Bictegravir	▪ STR once daily with FTC/TAF ▪ Few drug or food interactions ▪ High barrier to resistance	▪ Least amount of data ▪ Only available as an STR ▪ Limited safety data in pregnancy
Dolutegravir	▪ STR once daily with 3TC or 3TC/ABC ▪ Also available as a single agent (eg, can be combined with other NRTIs) ▪ Few drug or food interactions ▪ High barrier to resistance ▪ A preferred option for pregnant women and women trying to conceive[3]	▪ ABC coformulation requires HLA-B*5701 testing ▪ Increases metformin levels ▪ Limited safety data at conception[3]
Raltegravir	▪ Longest experience ▪ Few drug or food interactions ▪ A preferred option for pregnant women	▪ Multiple pills (ie, no STR) ▪ Lower barrier to resistance than BIC or DTG ▪ Limited safety data at conception ▪ Recommended as initial regimen only in certain clinical situations

1. DHHS ART Guidelines. June 2021. 2. Saag. JAMA. 2020; 324:1651. 3. DHHS Perinatal Guidelines. February 2021.

Single-Tablet Regimens Available for Initial ART

Class	Agent	Components	Caveats[1]
INSTI	BIC/FTC/TAF	INSTI + dual NRTI	
	DTG/3TC	INSTI + single NRTI	Do not use if HIV-1 RNA > 500,000 c/mL, HBV coinfection, or without resistance testing results
	DTG/3TC/ABC	INSTI + dual NRTI	Only if HLA-B*5701 negative
	EVG/COBI/FTC/(TAF or TDF)	Boosted INSTI + dual NRTI	
NNRTI	DOR/3TC/TDF	NNRTI + dual NRTI	
	EFV (400 or 600 mg)/3TC/TDF	NNRTI + dual NRTI	
	EFV/FTC/TDF	NNRTI + dual NRTI	
	RPV/FTC/(TAF or TDF)	NNRTI + dual NRTI	Only if HIV-1 RNA < 100,000 c/mL and CD4+ cell count > 200 cells/mm^3
Boosted PI	DRV/COBI/FTC/TAF	Boosted PI + dual NRTI	

1. DHHS Guidelines. December 2019.

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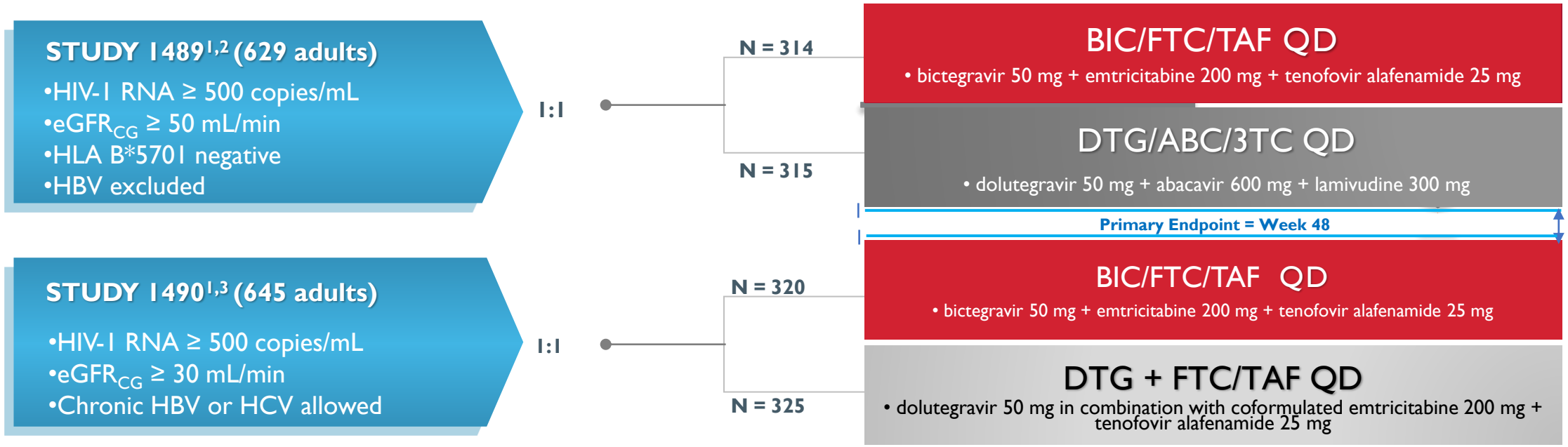
BIC/FTC/TAF 1489 and 1490 Studies

- Efficacy and safety are based on analyses of 48-week data from 2 RCTs in treatment-naïve HIV-1-infected adults (N = 1274)
- 1ry end point = Proportion with HIV-1 RNA <50 c/mL at wk 48
- Stratified by baseline HIV-1 RNA (≤100,000, >100,000, ≤400,000 c/mL, >400,000 c/mL), by CD4 (<50, 50-199, or ≥200 cells/mm^3)



DTG/ABC/3TC = dolutegravir, abacavir, and lamivudine.
DTG + FTC/TAF = dolutegravir + emtricitabine and tenofovir alafenamide; eGFR$_{CG}$ = estimated glomerular filtration rate; QD = once daily

1. Gallant J, et al. *Lancet*. 2017;390::2063-2072. 2. Sax PE, et al. Lancet. 2017;390::2073-2082.

Studies 1489 and1490: Selected Baseline Characteristics

	Study 1489[1,2]		Study 1490[1,3]	
	BIC/FTC/TAF (n = 314)	DTG/ABC/ 3TC (n = 315)	BIC/FTC/TAF (n = 320)	DTG + FTC/TAF (n = 325)
Median age, years (range)	31 (18-71)	32 (18-68)	33 (27-46)	34 (27-46)
Sex				
Male (%)	91	90	88	89
Female (%)	9	10	13	11
Race/ethnicity				
White (%)	57	57	57	60
Black or African descent (%)	36	36	30	31
Hispanic/Latino ethnicity (%)	23	21	26	25
Asian (%)	2	3	2	3
Median HIV-1 RNA, $\log_{10}$ copies/mL	4.42	4.51	4.43	4.45
HIV-1 RNA >100,000 copies/mL (%)	17	16	17	13
Median CD4+ cell count, cells/mm^3	443	450	440	441
Median $eGFR_{CG,}$ mL/min	125.9	123.0	120.4	120.6
Patients with HIV/HBV co-infection (%)	N/A	N/A	3	2
Patients with HCV/HBV co-infection (%)	N/A	N/A	2	2

1. Gallant J, et al. *Lancet*. 2017;390::2063-2072. 2. Sax PE, et al. Lancet. 2017;390::2073-2082.

Studies 1489 and 1490 Virologic Outcomes at Week 48

	BIC/FTC/TAF (n = 634)	DTG/ABC/3TC (n = 315)	DTG + FTC/TAF (n = 325)
HIV-1 RNA < 50 copies/mL	91%	93%	93%
Treatment Difference (95% CI) B/F/TAF vs. Comparator	-	-2.1% (-5.9% to 1.6%)	-1.9% (-5.6% to 1.8%)
HIV-1 RNA ≥ 50 copies/mL	3%	3%	1%
No Virologic Data at Week 48 Window	6%	4%	6%
Discontinued study drug due to AE or death	< 1%	1%	1%
Discontinued study drug due to other reasons and last available HIV-RNA <50 c/mL	4%	3%	4%
Missing data during window but on study drug	2%	<1%	1%

- BIC/FTC/TAF was non-inferior in achieving HIV-1 RNA < 50 copies/mL at Week 48 when compared to ABC/DTG/3TC and DTG + FTC/TAF, respectively.

1. Gallant J, et al. *Lancet*. 2017;390::2063-2072. 2. Sax PE, et al. Lancet. 2017;390::2073-2082.

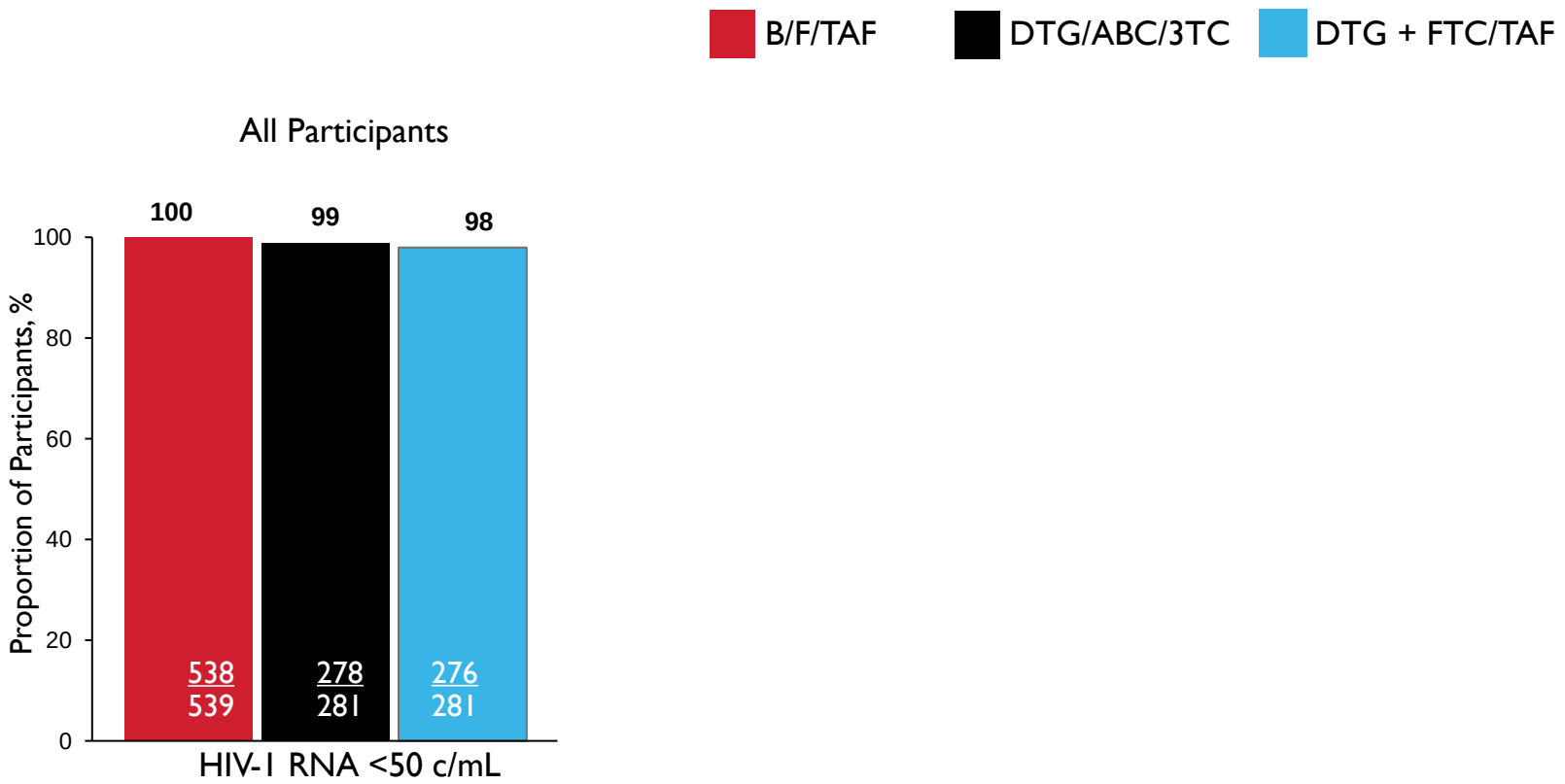
Studies 1489 and 1490 Virologic Outcomes at Week 48

	BIC/FTC/TAF (n = 634)	DTG/ABC/3TC (n = 315)	DTG + FTC/TAF (n = 325)
Proportion (%) of Patients with HIV-1 RNA < 50 c/mL by Subgroup			
By Baseline Viral Load			
≤ 100,000 c/mL	92%	94%	93%
> 100,000 c/mL	87%	90%	94%
By Baseline CD4 Cell Count			
< 200 cells/mm^3	90%	81%	100%
≥ 200 cells/mm^3	91%	94%	92%
HIV-1 RNA < 20 copies/mL	85%	87%	87%
Mean Increase from Baseline CD4 (cells/mm^3)	207	229	201

- Treatment outcomes were similar across subgroups, regardless of age, sex, race, baseline viral load, and baseline CD4+ cell count

1. Gallant J, et al. *Lancet*. 2017;390::2063-2072. 2. Sax PE, et al. Lancet. 2017;390::2073-2082.

Outcomes by Baseline HIV-1 RNA and CD4 at Week 96 by Pooled Per-Protocol Analysis

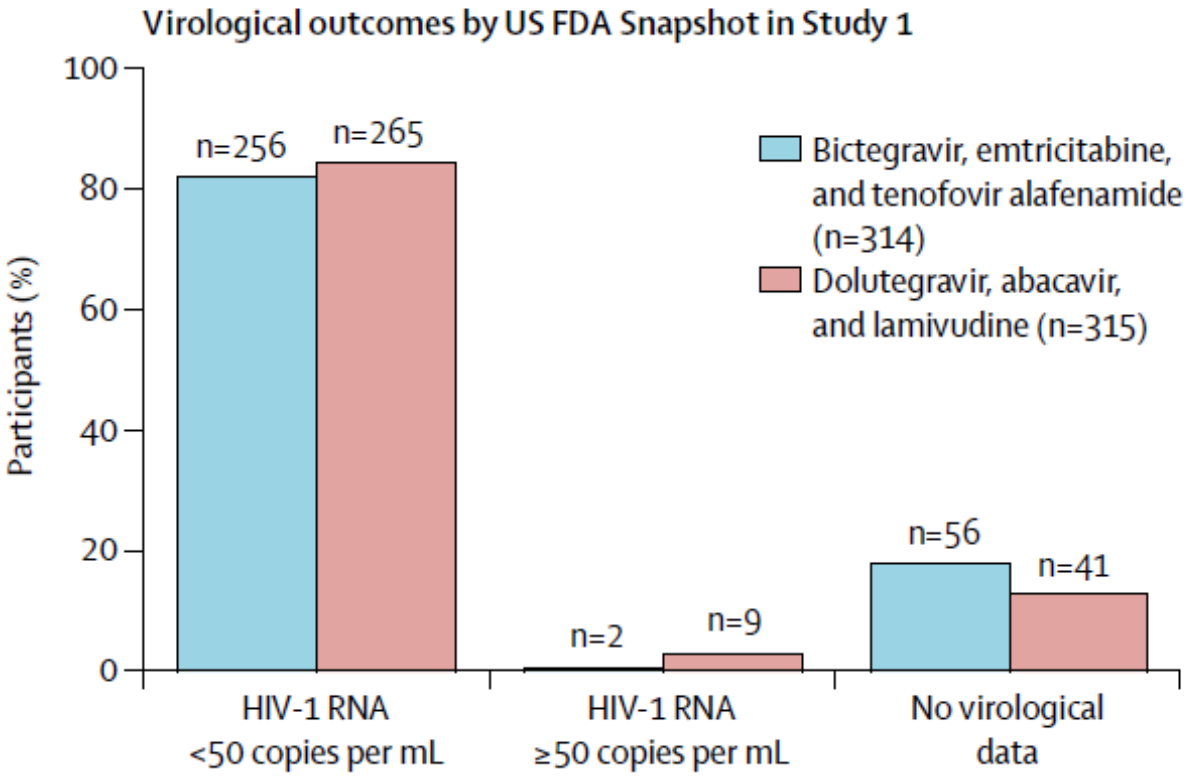


No participants discontinued due to lack of efficacy

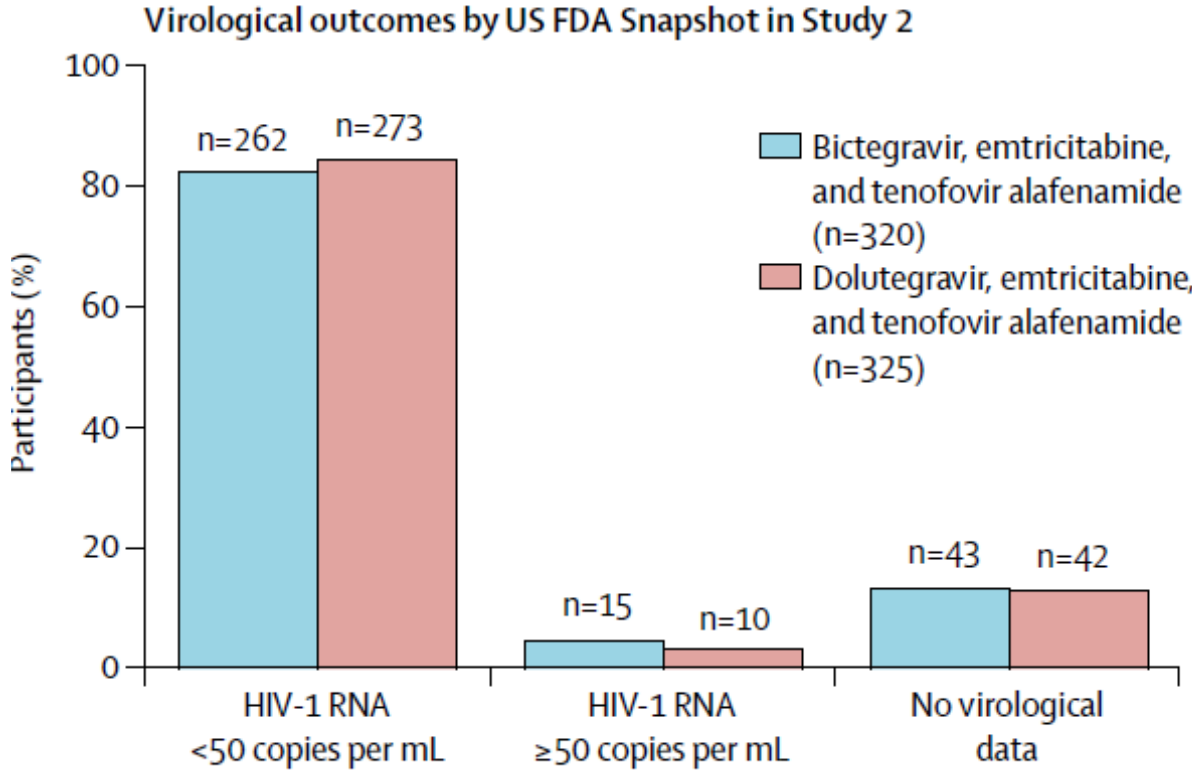
No participants developed emergent resistance

BIC/FTC/TAF 1489 and 1490 Studies: Outcomes at Week 144

Study 1489



Study 1490

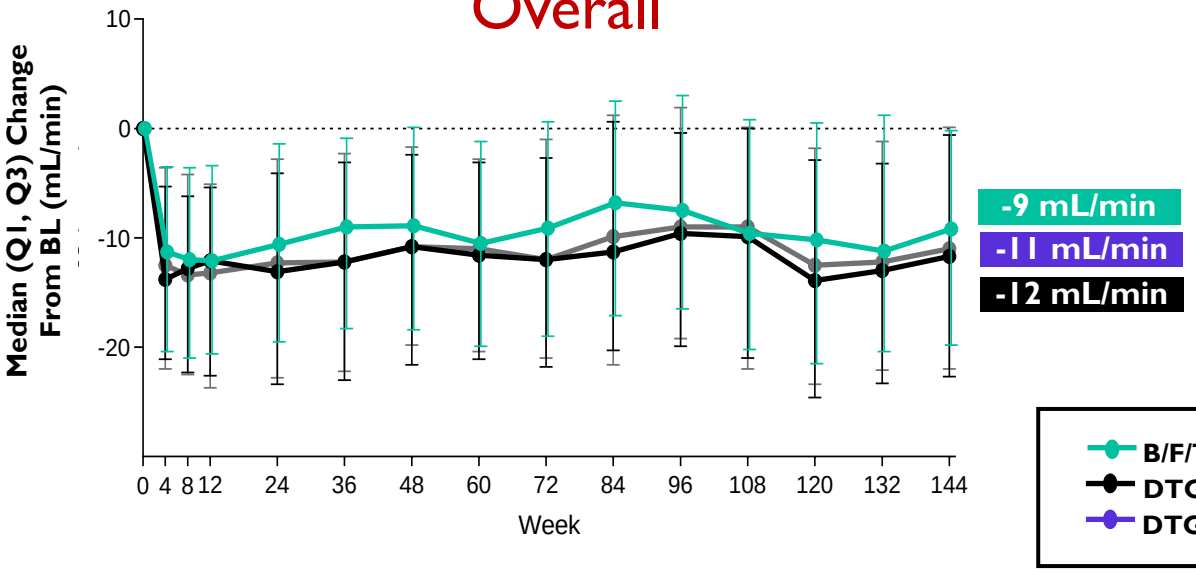


Initial treatment with B/F/TAF was noninferior to DTG-based triple therapy regimens at Week 144, with high rates of virologic suppression in all treatment arms

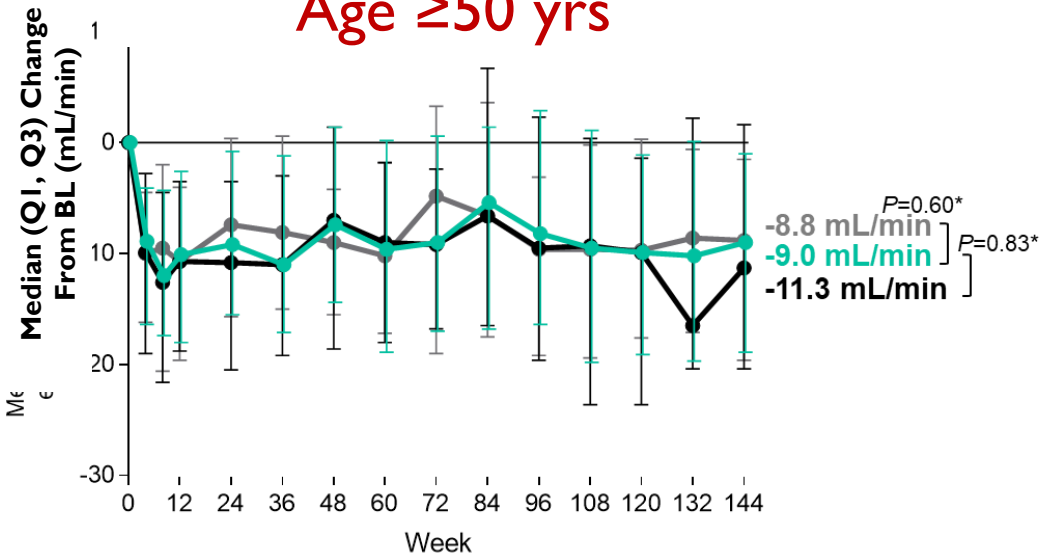
Orkin C, et al. Lancet HIV 2020 ; 7 : e389-400.

BIC/FTC/TAF 1489 and 1490 Studies: eGFR Change by Visit

Pooled 1489 and 1490[1]
Overall



Pooled 1489 and 1490[2]
Age ≥50 yrs



- Changes from baseline in eGFR were comparable between B/F/TAF and DTG/ABC/3TC in ART-naïve adults
  - No statistically significant difference between B/F/TAF and comparators in adults ≥50 years
- eGFR decline in virologically suppressed adults ≥65 years is consistent with known inhibition of OCT2 creatinine transporter

1. Orkin C, et al. EACS 2019. Basel, Switzerland. PE3/14 2. Mills A, et al. CROI 2020. Boston, MA. 477

BIC/FTC/TAF 1489 and 1490 Studies: Bone Safety in Women through Week 144

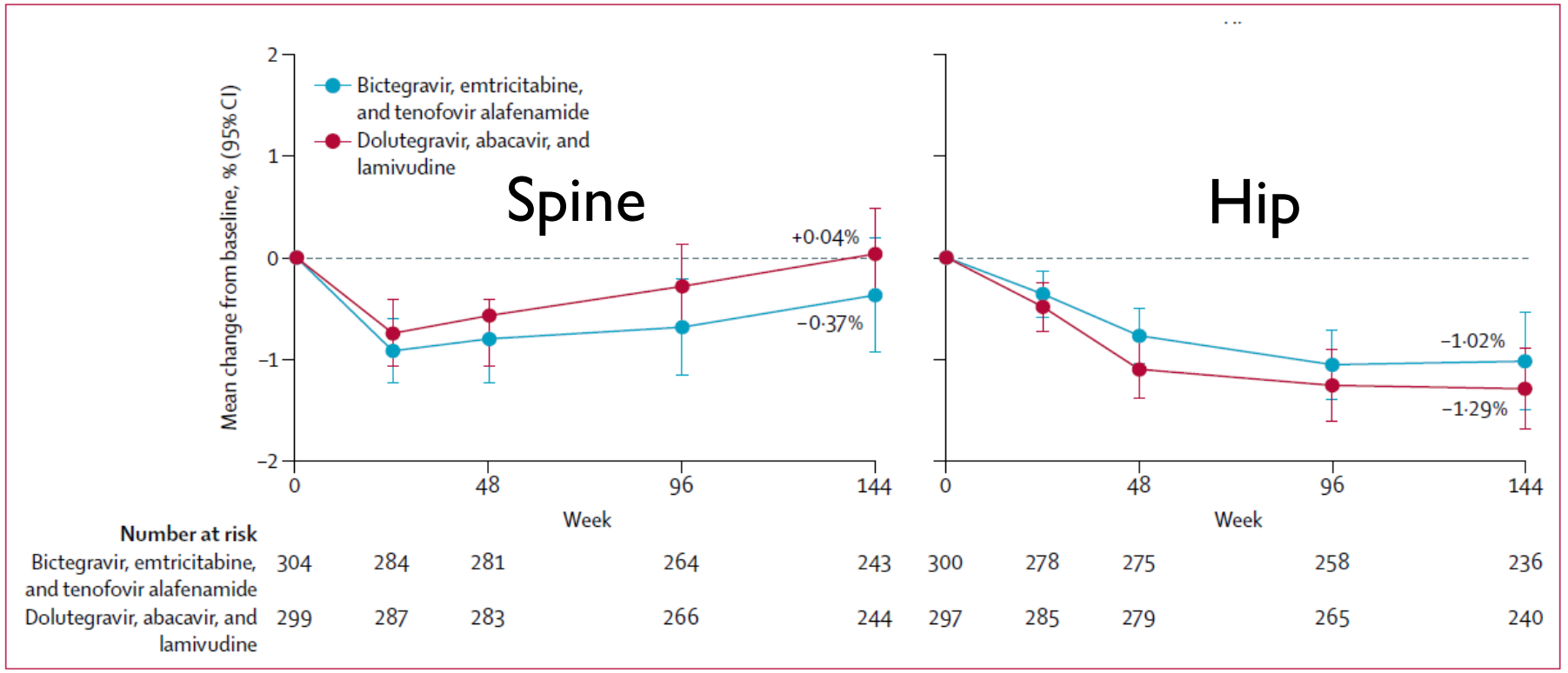


Figure 4: Mean percent change from baseline at weeks 24, 48, 96, and 144 in lumbar spine and hip bone mineral density by DXA in Study 1
Bars show 95% CIs.

Changes from baseline in BMD were comparable between B/F/TAF vs DTG/ABC/3TC in treatment-naïve women

Orkin C, et al. Lancet HIV 2020 ; 7 : e389-400.

BIC and DTG Triple Therapy for Initial ART:
3-year Resistance and Efficacy in Patients with BL Resistance

- Retrospective BL next-generation sequencing of samples from participants treated with BIC/FTC/TAF, DTG/ABC/3TC, or DTG + FTC/TAF in Studies 1489 and 1490

RAS at baseline	BIC/FTC/TAF (n=634)		DTG/ABC/3TC (n=315)		DTG + FTC/TAF (n=325)	
	No. (%)	HIV RNA <50 c/mL, %	No. (%)	HIV RNA <50 c/mL, %	No. (%)	HIV RNA <50 c/mL, %
Primary NRTI associated	21 (3.3)	100	8 (2.5)	100	6 (1.8)	100
Primary INSTI associated	7 (1.1)	100	4 (1.3)	75.0	6 (1.9)	100
Secondary INSTI associated	326 (51.6)	98.1	152 (48.4)	95.4	161 (49.7)	96.9
Primary NNRTI associated	82 (12.9)	98.8	53 (16.8)	98.1	45 (13.8)	97.8
Primary PI associated	19 (3.0)	100	13 (4.1)	92.3	12 (3.7)	100

- 1 person in BIC/FTC/TAF group had preexisting BIC and DTG RAMs (Q148H and G140S)
  - Achieved viral suppression and maintained HIV RNA <50 copies/mL through Wk 144
- No emergent resistance to study drugs

Acosta RK. J Antimicrob Chemother 2021;76:2153-7.

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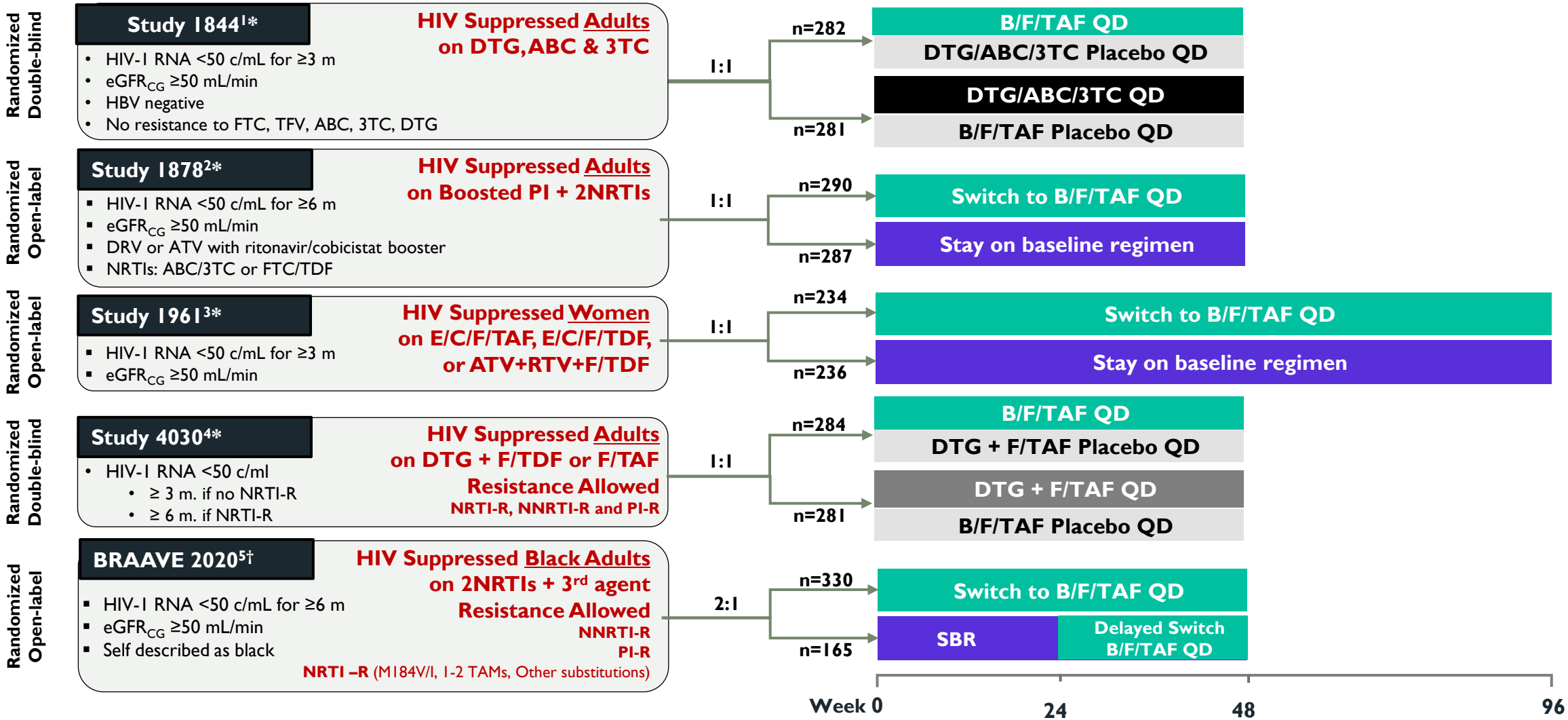
Clinical Data of BIC/FTC/TAF* on Treatment-naïve Patients

Clinical Data of BIC/FTC/TAF on Treatment-experienced Patients

*Bictegravir, Emtricitabine, and Tenofovir Alafenamide

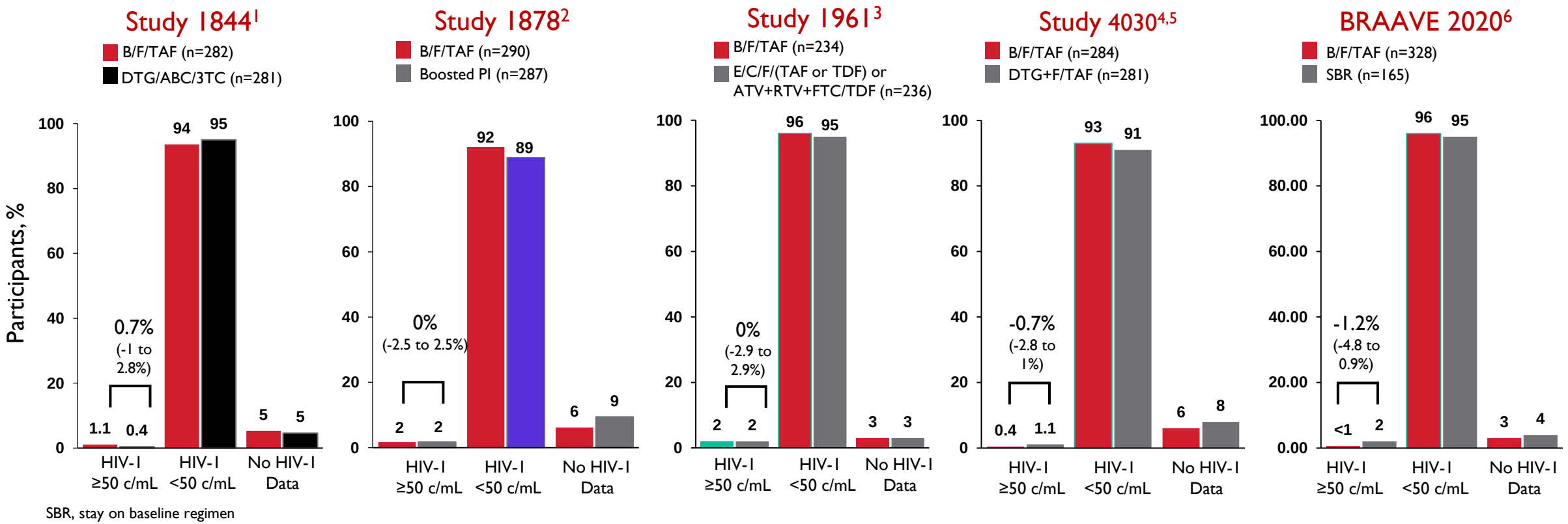
Studies of BIC/FTC/TAF on Treatment-experienced Patients



*Primary endpoint: HIV-1 RNA <50 c/mL at W48 (Snapshot; 4% non-inferiority margin)†Primary endpoint: HIV-1 RNA <50 c/mL at W24 (Snapshot; 6% non-inferiority margin)

1. Molina JM, et al. *Lancet* HIV 2018;5:e357–65; 2. Daar E, et al. *Lancet* HIV 2018;5:e347–56; 3. Kityo C, et al. JAIDS 2019. 82(3):321-328; 4. Acosta R, et al. IAS 2019. Mexico City. Poster MOPEB241; 5. Hagins D, et al. JAIDS 2021

Virologic Outcome by FDA Snapshot Analysis



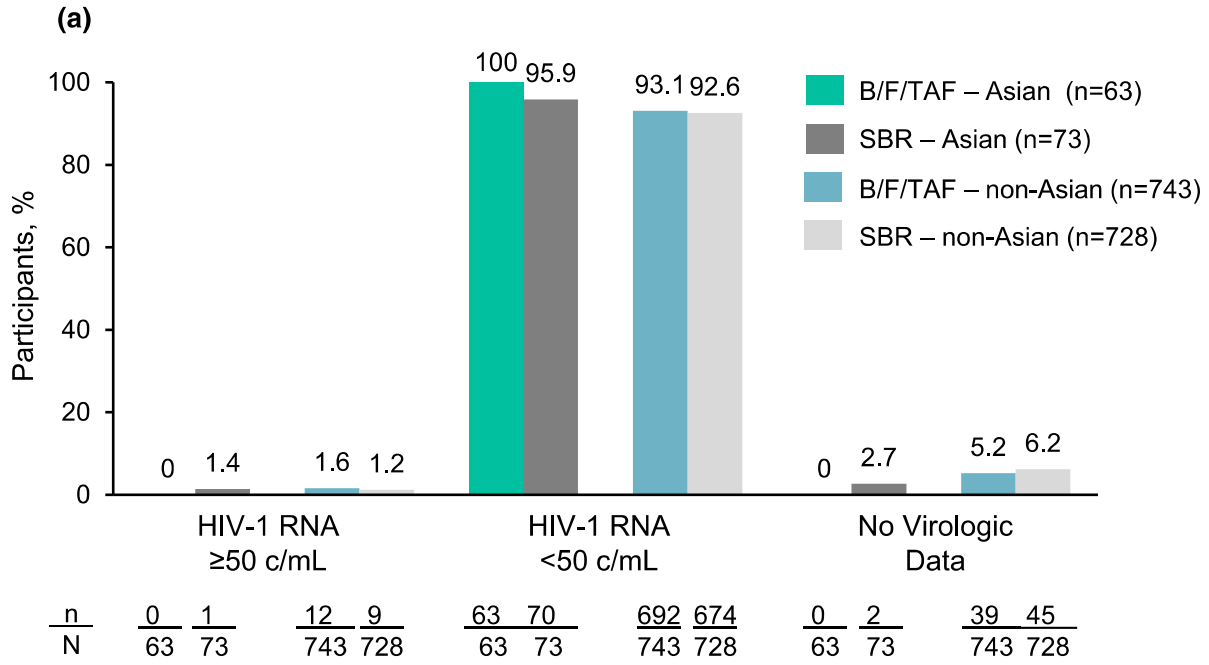
SBR, stay on baseline regimen

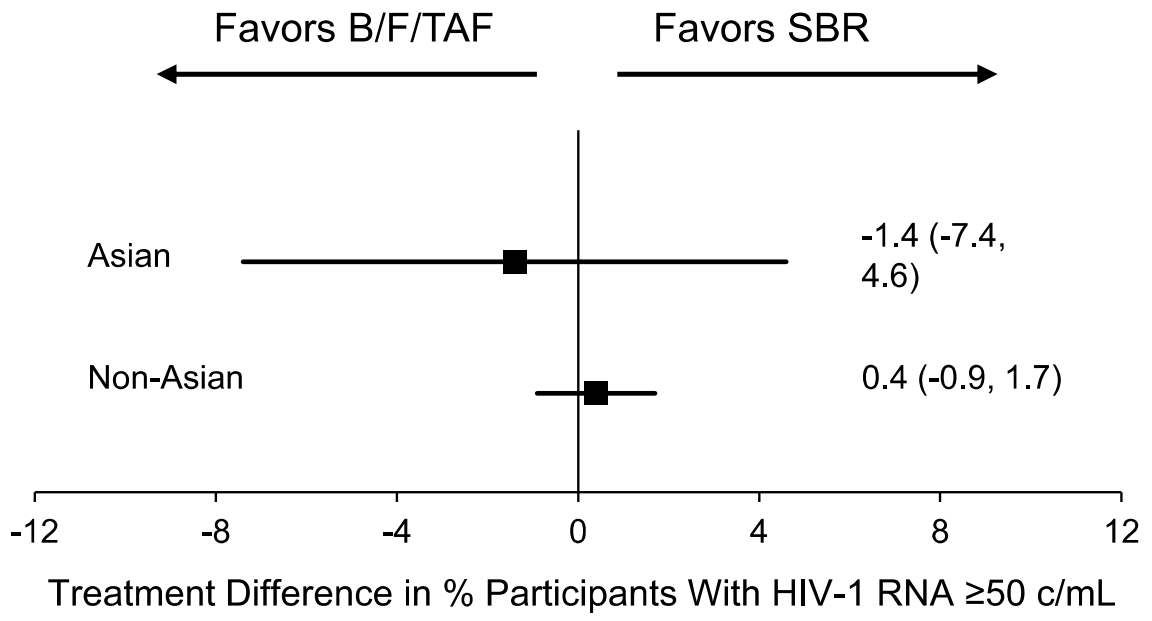
Switching to TAF has non-inferior efficacy in all suppressed adults switched from multiple regimens through W24 and w48

1. Molina JM, et al. *Lancet* HIV 2018;5:e357–65
2. Daar E, et al. *Lancet* HIV 2018;5:e347–56.
3. Kityo C, et al. JAIDS 2019. 82(3):321-328
4. Acosta R, et al. IAS 2019. Mexico City. Poster MOPEB241
5. Sax P. et al. IAS 2019. Mexico City. Oral MOAB0105
6. Hagins D, et al. JAIDS 2021

Switching to BIC/FTC/TAF in Virologically Suppressed Asians

- Pooled analysis of virologically suppressed Asians from 3 international phase III trials to evaluate efficacy and safety of switching to B/F/TAF.
- 1ry endpoint: Plasma HIV-1 RNA ≥50 c/ml at week 48
  - 0% B/F/TAF vs 1.4% stayed on baseline regimens.
- Virological suppression: 100% B/F/TAF vs. 96% stayed on baseline regimens (p = 0.2485)





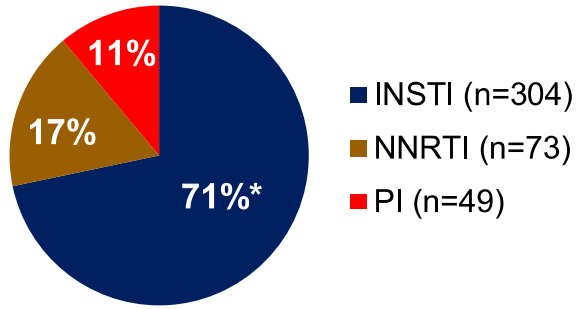
Avihingsanon A, et al. HIV Medicine 2022;1–11.

BIC/FTC/TAF: 12-month Real World Effectiveness in Treatment-naïve and -experienced PLHIV

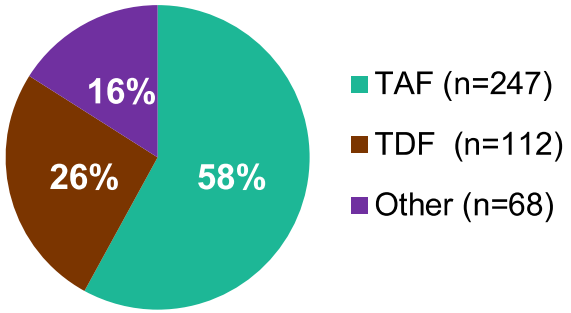
Baseline Characteristics

		TN, n=84	TE, n=429
Demographics	Male, n (%)	76 (91)	392 (91)
	Age, years, median (Q1–Q3)	38 (29–48)	49 (40–56)
	Age ≥50 years, n (%)	20 (24)	209 (49)
	White, n (%)	71 (85)	387 (90)
Ongoing comorbidities	None, n (%)	41 (49)	108 (25)
	1–2, n (%)	25 (30)	168 (39)
	≥3, n (%)	18 (21)	153 (36)
	Neuropsychiatric disorder[a], n (%)	16 (19)	122 (28)
	Hyperlipidaemia, n (%)	7 (8)	87 (20)
	Hypertension, n (%)	5 (6)	87 (20)
HIV-related characteristics	HIV-1 RNA, log_{10} cp/mL, median (Q1, Q3)	4.77 (3.94, 5.18)	1.59 (1.28, 1.59)
	<50 cp/mL, n (%)	0 (0)	362/393 (92)
	>100,000 cp/mL, n (%)	30/82 (37)	2/393 (1)
	CD4 count[b], cells/µL, median (Q1, Q3)	427 (244, 581)	668 (455, 877)
	CD4 <200 cells/µL, %	21	4
	CD4 <350 cells/µL, %	38	14
	CD4/CD8 ratio, median (Q1, Q3)	0.4 (0.3, 0.6)	0.8 (0.6, 1.2)
	≥1 major mutation[c], n (%)	7 (9)	36 (9)
	PI / NNRTI / NRTI / INSTI, n (%)	2 (2) / 5 (6) / 1 (1) / 0	12 (3) / 20 (5) / 16 (4) / 1 (0.3)

Prior ART Regimens (n=427)



*DTG, 34%; EVG, 24%; RAL, 14%;
1 participant without third agent

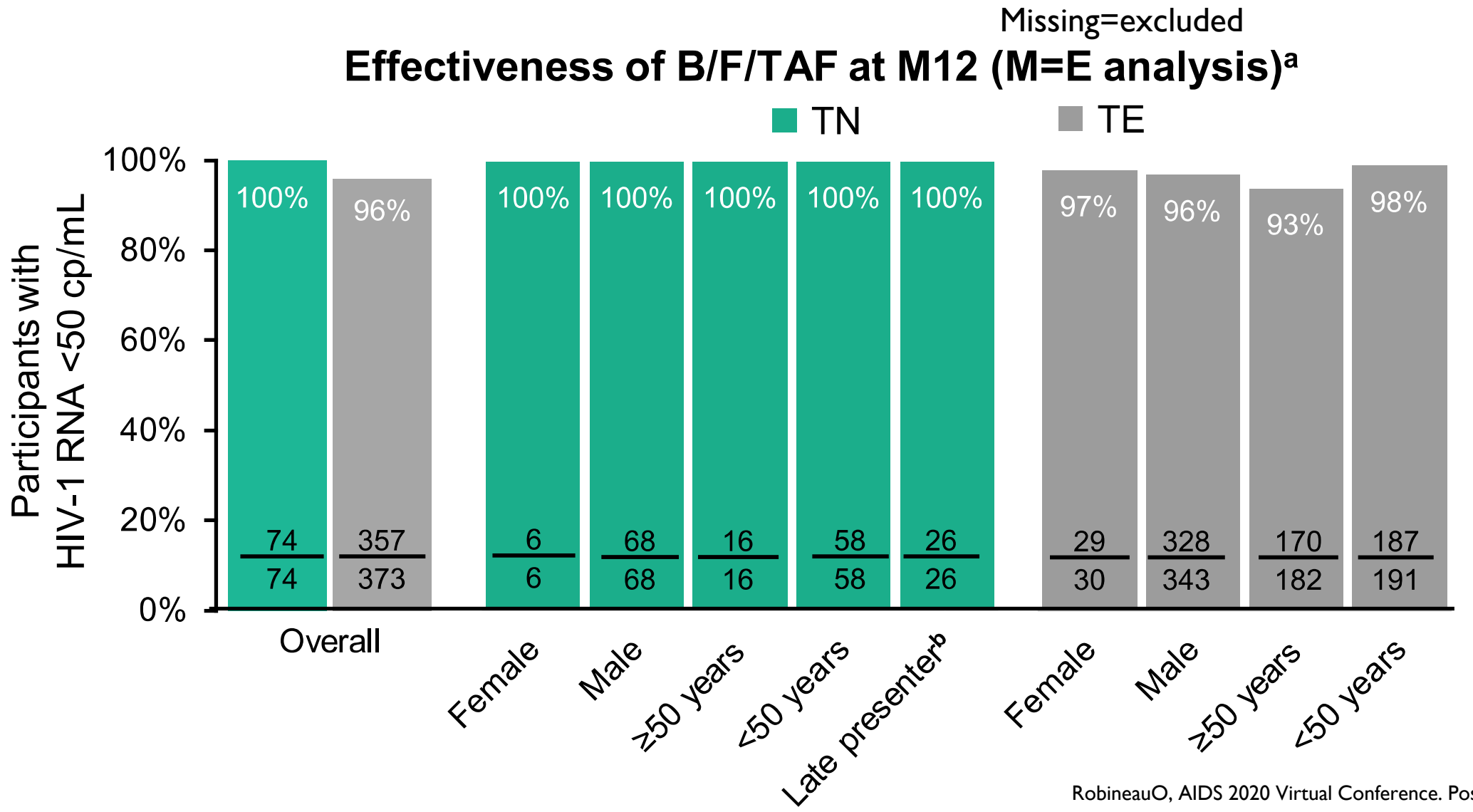


[a]Most common neuropsychiatric disorders at baseline were insomnia 2.9%, depression 1.6% and anxiety 1.4%; [b]Sample size of 78 for TN and 382 for TE; [c]A participant could have >1 mutation/substitution

ART, antiretroviral treatment; cp, copies; DTG, dolutegravir; EVG, elvitegravir; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleo[s/t]ide reverse transcriptase inhibitor; PI, protease inhibitor; Q, quartile; RAL, raltegravir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TE, treatment experienced; TN, treatment naïve

RobineauO, AIDS 2020 Virtual Conference. Poster PEB0229.

BIC/FTC/TAF: 12-month Real World Effectiveness in Treatment-naïve and -experienced PLHIV



RobineauO, AIDS 2020 Virtual Conference. Poster PEB0229.

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Thank you