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Biktarvy® (BIC/FTC/TAF) Efficacy and Safety by Baseline CD4

This document is in response to your request for information on the efficacy and general safety profile of Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) by baseline (BL) cluster of differentiation 4 (CD4) cell count in antiretroviral (ARV)-naive people with HIV (PWH).

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Summary

Clinical Data: BIC/FTC/TAF in PWH by BL CD4 Count

Studies GS-US-380-1489 (Study 1489) and GS-US-380-1490 (Study 1490) compared the efficacy and safety of BIC/FTC/TAF to DTG-containing regimens (DTG/ABC/3TC or DTG + FTC/TAF) in ARV-naive adult PWH.[1,2] In a pooled analysis, BIC/FTC/TAF demonstrated non-inferior efficacy (HIV-1 RNA <50 c/mL) to triple therapy DTG-containing regimens by FDA Snapshot at Week 144 among participants with CD4 <200 cells/mcL at BL (BIC/FTC/TAF, 100%; DTG/ABC/3TC, 92%; DTG + FTC/TAF, 100%).[3] No significant differences in efficacy were observed in subgroups by BL CD4 cell count at Week 48 or 144.[4-6] In participants who were randomly assigned to BIC/FTC/TAF, high rates of virologic suppression were maintained at Week 240 regardless of CD4 cell count.[7]

In the LAPTOP study, which assessed the efficacy and safety of BIC/FTC/TAF (n=220) vs DRV/c/FTC/TAF (n=222) in ARV-naive adults with advanced HIV-1, BIC/FTC/TAF was non-inferior to DRV/c/FTC/TAF in the composite endpoint of virologic failure or clinical events.[8]

RWD: BIC/FTC/TAF in PWH by BL CD4 Count

In a study of patients with a BL CD4 cell count ≤200 cells/mcL, patients treated with BIC/FTC/TAF were more likely to recover a CD4 cell count >200 cells/mcL and achieve virologic suppression than patients on a boosted regimen.[9]

In a retrospective study of patients with a BL CD4 cell count ≤200 cells/mcL, treatment with BIC/FTC/TAF resulted in high rates of virologic suppression at Week 24.[10]

In a retrospective cohort study, 84.6% of patients with a BL CD4 cell count ≤200 cells/mcL achieved virologic suppression with 24 weeks of BIC/FTC/TAF treatment.[11]

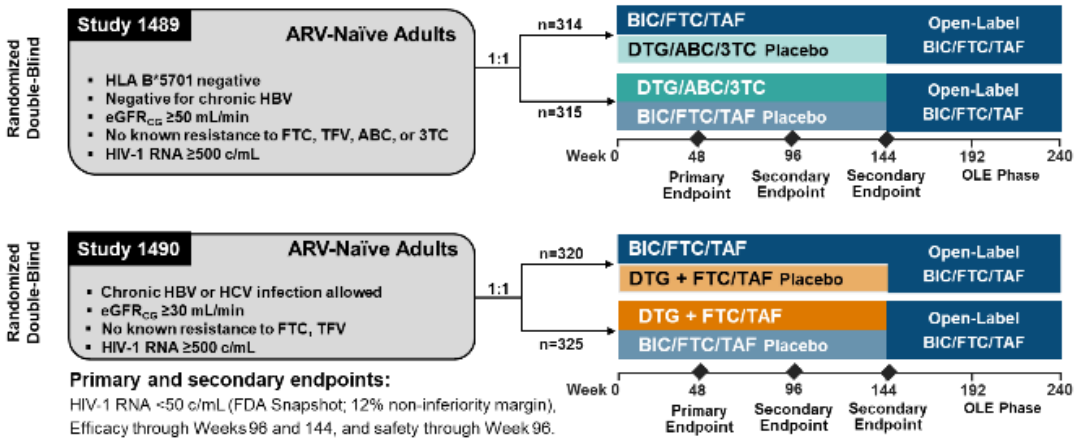
Clinical Data: BIC/FTC/TAF in PWH by BL CD4 Count

Studies 1489 and 1490

Study designs and demographics

Studies 1489 and 1490 compared BIC/FTC/TAF to DTG-containing regimens (Figure 1).[1,2] Participants transitioned into the open-label phase after the last participant reached Week 144. A pooled analysis of Studies 1489 and 1490 was also conducted. BL characteristics were similar between treatment groups (Table 1).[3,4]

Figure 1. Studies 1489 and 1490: Study Designs[3]



Abbreviations: $eGFR_{CG}$=eGFR by Cockcroft-Gault; HLA=human leukocyte antigen; OLE=open-label extension; TFV=tenofovir.

Table 1. Studies 1489 and 1490: BL Demographics and Disease Characteristics[12]

Key Demographics and Characteristics	BIC/FTC/TAF (n=634)	DTG/ABC/3TC (n=315)	DTG + FTC/TAF (n=325)
Age, median (range), years	32 (18–71)	32 (18–68)	34 (18–77)
Male, %	89	90	89
CD4 count <200 cells/mcL, %	13	10	10

Efficacy results through Week 144

BIC/FTC/TAF demonstrated non-inferior efficacy to DTG/ABC/3TC in Study 1489 (92% vs 93%; *P*=0.78) and to DTG + FTC/TAF in Study 1490 (89% vs 93%; *P*=0.12) by FDA Snapshot analysis at the Week 48 primary endpoint.[5,6] Participants who received BIC/FTC/TAF had high response rates regardless of low CD4 count (99%) or both high VL and low CD4 count (97%) at BL.[12] High rates of virologic suppression were maintained at Week 144, and BIC/FTC/TAF remained non-inferior to both DTG-based regimens. Treatment-emergent resistance was not detected in any treatment group.[4]

Safety results through Week 144

AEs are provided in Table 2 below. There were no reports of proximal renal tubulopathy in any arm and no discontinuations due to renal AEs on BIC/FTC/TAF.[4]

Table 2. Studies 1489 and 1490: Safety Results at Week 144[3,4]

AEs, %		BIC/FTC/TAF (n=634)	DTG/ABC/3TC (n=315)	DTG + FTC/TAF (n=325)
Serious AE		16	17	12
AEs occurring ≥5% of any group	Nausea	4	18	5
	Headache	5	5	3
	Diarrhea	5	4	3
AE leading to discontinuation		1	2	2

Week 240 pooled analysis[7]

A pooled analysis that included all BIC/FTC/TAF-treated participants through Week 240 was conducted. BL demographics and disease characteristics are shown in Table 3.

Table 3. Studies 1489 and 1490 Week 240 Pooled Analysis: BL Demographics of BTC/FTC/TAF-Treated Participants by BL Stratification[7]

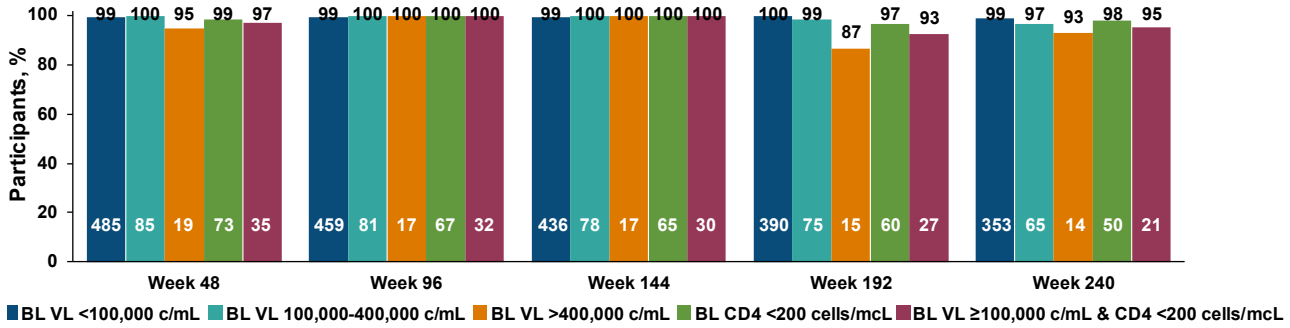
	BL VL <100,000 c/mL (n=515)	BL VL 100,000–400,000 c/mL (n=99)	BL VL >400,000 c/mL (n=20)	BL CD4 ≥200 cells/mcL (n=554)	BL CD4 <200 cells/mcL (n=80)	BL VL ≥100,000 c/mL & CD4 <200 cells/mcL (n=39)
Age, median (range), years	32 (18–71)	33 (18–71)	35 (23–68)	31 (18–71)	36 (22–64)	36 (22–64)
Female at birth, n (%)	64 (12)	5 (5)	0	59 (11)	10 (13)	1 (3)
Body weight, median (Q1, Q3), kg	77.5 (68.2, 89.2)	74.8 (66.7, 84.8)	73.9 (64.9, 83.3)	77.2 (68.2, 88)	71.5 (64.5, 84.7)	71.9 (63.5, 85.3)

Abbreviation: Q=quartile.

Efficacy

High rates of virologic suppression were maintained through Week 240, regardless of BL HIV-1 RNA and CD4 count (missing=excluded; Figure 2). No participants developed treatment-emergent resistance to BIC, FTC, or TAF.

Figure 2. Studies 1489 and 1490 Week 240 Pooled Analysis: HIV-1 RNA <50 c/mL Through Week 240 by BL Stratification[7]



At Week 240, 77/80 participants with BL CD4 <200 cells/mcL had CD4 ≥200 cells/mcL. Three participants continued to have a CD4 count <200 cells/mcL (183, 180, and 111 cells/mcL) at Week 240, but each attained virologic suppression by Week 4 and remained suppressed through Week 240.

Safety

Safety results are provided in Table 4. Five cases of immune reconstitution inflammatory syndrome were reported: 2 occurred among participants who had a CD4 <200 cells/mcL at BL; all occurred within the first 48 weeks, and all resolved with treatment.

Table 4. Studies 1489 and 1490 Week 240 Pooled Analysis: Safety Results Through Week 240 According to BL Stratification[7]

AEs, %		BL VL <100,000 c/mL (n=515)	BL VL 100,000–400,000 c/mL (n=99)	BL VL >400,000 c/mL (n=20)	BL CD4 <200 cells/mcL (n=80)	BL VL ≥100,000 c/mL & CD4 <200 cells/mcL (n=39)
Any drug-related AE		28	30	20	25	21
Drug-related AEs that occurred in ≥5% of participants	Nausea	5	4	0	4	3
	Headache	4	7	10	8	10
	Diarrhea	4	7	10	6	8
	Dizziness	2	3	5	0	0
AEs that led to discontinuation of study drug		2	1	0	3	0

Weight changes

At Week 48, participants who had a CD4 count <200 cells/mcL at BL had significantly greater median changes in weight from BL than those who had a CD4 count ≥200 cells/mcL (8.3 kg vs 2.7 kg; *P*<0.001). The median actual weights at Week 240 were comparable across subgroups, despite BL values that were significantly lower in the CD4 <200 cells/mcL subgroup than in the CD4 ≥200 cells/mcL subgroup (71.2 kg vs 77 kg; *P*<0.05).

LAPTOP Study: BIC/FTC/TAF vs DRV/c/FTC/TAF in People With Advanced HIV[8]

Study design and demographics

A European, multicenter, open-label, randomized, controlled, non-inferiority study was conducted to assess the efficacy and safety of BIC/FTC/TAF (n=220) vs DRV/c/FTC/TAF (n=222) in ARV-naive adults with advanced HIV-1. Eligible participants had HIV-1 RNA >1000 c/mL and AIDS with any CD4 cell count, a severe BI with a CD4 count <200 cells/mcL, a CD4 count <100 cells/mcL with or without symptoms, or a serious OI under treatment at the time of enrollment. The primary outcome was the time to failure, defined as the first occurrence of any composite of virologic failure (either insufficient virologic response [HIV-1 RNA reduction $<1_{log10}$ c/mL at Week 12] or HIV-1 RNA >50 c/mL at Week 48) or a clinical event. In addition, individual components were evaluated by Kaplan-Meier and Cox regression analyses.

Table 5. LAPTOP Study: BL Demographics and Disease Characteristics[8]

Key Demographics and Characteristics	Total (N=442)
Age, median (IQR), years	43 (35–53)
Male sex, n (%)	358 (81)
Race, White/Black/other, n (%)	276 (62.4)/83 (18.8)/83 (18.8)
CD4 count <100 cells/mcL, n (%)	379 (85.8)
HIV-1 RNA >500,000 c/mL, n (%)	197 (44.6)

Results

BIC/FTC/TAF was non-inferior to DRV/c/FTC/TAF in regard to the primary composite endpoint (Table 6). At Weeks 4, 8, and 12, significantly more participants achieved HIV-1 RNA <50 c/mL in the BIC/FTC/TAF group than in the DRV/c/FTC/TAF group (each week, *P*<0.0001); a higher number of participants who received BIC/FTC/TAF achieved HIV-1 RNA <50 c/mL at Week 48. Among participants with CD4 ≤200 cells/mcL at BL, there was no significant difference between treatment groups in the time to achieve CD4 >200 cells/mcL (aHR, 1.12; 95% CI: 0.89–1.41; *P*=0.339).

Table 6. LAPTOP Study: Primary Composite Endpoint and Components (mITT Analysis)[8]

Endpoint, n (%)	BIC/FTC/TAF (n=220)	DRV/c/FTC/TAF (n=222)	aHR (95% CI); *P*-Value
Primary composite endpoint	49 (23.8)	70 (33.9)	0.7 (0.48–1); 0.052
Virologic failure	25 (13.4)	46 (23.9)	0.54 (0.33—0.88); 0.013
Insufficient virologic response	23 (12.4)	43 (22.5)	0.53 (0.32–0.88); 0.014
Viral rebound	2 (1)	3 (1.5)	0.69 (0.12–4.15); 0.687
Clinical events	25 (11.8)	26 (12.1)	0.99 (0.57–1.72); 0.974
Any new/recurrent AIDS event within ≥28 days of therapy	7 (3.5)	15 (7.2)	0.48 (0.2–1.19); 0.114
SAE unrelated to AIDS events	11 (5.3)	5 (2.3)	2.32 (0.81–6.68); 0.119
AE that led to discontinuation	1 (0.5)	7 (3.3)	0.15 (0.02–1.18); 0.071
Death related to HIV, AIDS, or OI/BI	7 (3.3)	3 (1.4)	2.41 (0.62–9.33); 0.202

Abbreviation: mITT=modified intent-to-treat.
Note: The noninferiority margin was an HR of 1.606.

Overall, the incidence rates of Grade ≥2 AEs and drug-related Grade ≥2 AEs were significantly lower in the BIC/FTC/TAF group than in the DRV/c/FTC/TAF group (Table 7).

Table 7. LAPTOP Study: Select Safety Outcomes[8]

Parameter	BIC/FTC/TAF (n=220)	DRV/c/FTC/TAF (n=222)	Adjusted IRR (95% CI); *P*-Value
Any Grade ≥2 AEs, n	435	548	0.82 (0.73–0.93); 0.0024
Incidence rate per 100 PY	220.5	264.7	
Drug-related Grade ≥2 AEs, n	27	45	0.61 (0.38–0.98); 0.0431
Incidence rate per 100 PY	13.7	21.7	
Drug-related Grade 3–4 AEs, n	5	5	0.99 (0.29–3.44); 0.9931
Incidence rate per 100 PY	2.5	2.4	

Abbreviations: IRR=incidence rate ratio; PY=person-years.

RWD: BIC/FTC/TAF in PWH by BL CD4 Counts

OPERA Cohort: BL CD4 <200 cells/mcL[9]

An analysis was conducted among ARV-naive adults with CD4 <200 cells/mcL in the OPERA database. Patients initiated BIC/FTC/TAF (n=816), boosted darunavir (n=134), DTG (n=253), or boosted elvitegravir (n=146) regimens. Eligible patients had at least one CD4 cell count and VL assessment during follow-up. BL demographics were similar between groups. A total of 1349 PWH were included in the analysis, with varied durations of follow-up ranging from 10 to 36 months. A total of 1147/1349 patients (85%) achieved a CD4 cell count recovery ≥200 cells/mcL, 1147/1349 patients (85%) achieved virologic suppression (HIV-1 RNA <200 c/mL), and 947/1349 patients (70%) achieved virologic undetectability (HIV-1 RNA <50 c/mL). Patients receiving BIC/FTC/TAF were more likely to achieve a CD4 cell count ≥200 cells/mcL than patients in the other treatment groups.

Spanish HIV CORIS Cohort: BL CD4 <200 cells/mcL[10]

A retrospective comparison of virologic outcomes was conducted in patients with a BL CD4 count <200 cells/mcL who began BIC/FTC/TAF (n=95) or other ARV regimens (n=137). The primary outcome was the proportion of patients who achieved virologic suppression (HIV-1 RNA <50 c/mL) at Week 24, and the secondary outcome was an assessment of factors associated with the achievement of virologic suppression. BL demographics were similar between treatment groups: the median patient age was 39.8 years, the majority of the patients were male, and 24% had CD4 nadir <50 cells/mcL. Treatment with BIC/FTC/TAF resulted in higher rates of virologic suppression than did other ARV regimens at Week 24 (73.68% vs 59.85%; *P*=0.03); the probability of achieving virologic suppression was 1.9 times higher with BIC/FTC/TAF treatment than with other ARV regimens (95% CI: 1.1–3.3).

Retrospective Cohort Study in China[11]

A single-center, retrospective cohort study in China assessed the effectiveness and safety of BIC/FTC/TAF treatment in ARV-naive patients (N=80). Outcomes included the rate of virologic suppression (HIV-1 RNA <50 c/mL), CD4 cell counts, and the CD4/8 ratio after 24 weeks of treatment. At 24 weeks, 69 of 80 patients (86.3%) overall achieved virologic suppression; rates of virologic suppression among patients with a BL CD4 cell count ≤200 and >200 cells/mcL were 84.6% and 87.8%, respectively. From BL to 24 weeks, overall median (IQR) CD4 cell counts increased from 212 (90.3–398.3) cells/mcL to 348 (219.8–541) cells/mcL, and the CD4/8 ratio increased from 0.25 (0.13–0.37) to 0.4 (0.26–0.66). Patients with a CD4 count ≤200 cells/mcL at BL had an increase in CD4 cell counts from 82 (29.5–141) cells/mcL to 225 (119.5–293) cells/mcL and an increase in CD4/8 ratio from 0.13 (0.08–0.22) to 0.28 (0.18–0.4) from BL to Week 24. Patients with BL CD4 cell counts >200 cells/mcL had an increase from 397 (291–484) cells/mcL to 488 (409–663) mcL and an increase in CD4/8 ratio from 0.34 (0.25–0.49) to 0.64 (0.4–0.79) at Week 24.

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Abbreviations

3TC=lamivudine
ABC=abacavir
AE=adverse event
aHR=adjusted hazard ratio
ARV=antiretroviral
BI=bacterial infection
BIC=bictegravir
BL=baseline
c/mL=copies/mL
CD4/8=cluster of differentiation 4/8
CORIS=Cohort de la Red de Investigacíon en Sida
DRV/c=darunavir/cobicistat
DTG=dolutegravir
FTC=emtricitabine
OI=opportunistic infection
OPERA=Observational Pharmaco-Epidemiology Research and Analysis
PWH=people with HIV
RWD=real-world data
TAF=tenofovir alafenamide
VL=viral load

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Biktarvy US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi.

Follow-Up

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