GILEAD | Medical Information

# Biktarvy® (BIC/FTC/TAF) Use in Pediatric Patients

This document is in response to your request for information regarding the use of Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide [BIC/FTC/TAF]) in pediatric patients with HIV-1.

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**The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi.**

## Summary


### Product Labeling[1]

BIC/FTC/TAF is indicated as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥14 kg:

- with no ARV treatment history or
- with an ARV treatment history and not virologically suppressed, with no known or suspected substitutions associated with resistance to the INSTI class, FTC, or TFV, or
- to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA <50 c/mL) on a stable ARV regimen with no known or suspected substitutions associated with resistance to BIC or TFV.

### Clinical Data on BIC/FTC/TAF Use in Pediatric Participants

In an open-label study, the safety and efficacy of BIC/FTC/TAF treatment were evaluated in three cohorts of virologically suppressed children and adolescents living with HIV-1.[2,3]

- In Cohorts 1 and 2, PK results were either similar to those seen in adults, or differences were not considered clinically significant. Through Week 96, 5 Grade 3/4 AEs were reported, and 1 participant experienced an AE that led to study drug discontinuation. Virologic suppression was maintained across both cohorts with no treatment-emergent resistance through Week 96.[2,3]
- In Cohort 3, participants were treated with BIC/FTC/TAF 30/120/15 mg STR, and BIC, FTC, and TAF exposures ($AUC_T$) in this population were generally consistent with the ranges of exposures observed in adults. Of the 22 participants who were included in this analysis, 18 experienced AEs of any grade through Week 48. No AEs were Grade 3 or 4, were serious, or led to study drug discontinuation. Virologic suppression was maintained through Week 96 in all participants.[4]

In one pooled analysis of pediatric participants, 41% had ≥1 preexisting RAM, and virologic suppression rates were durable, including among participants with preexisting RAMs.[5,6]

In another pooled analysis of pediatric participants who switched to FTC/TAF-based treatment, changes in weight, height, and BMI from baseline to Week 48 of BIC/FTC/TAF

treatment were consistent with age-expected child development, and TC, LDL, and TG levels improved.[7,8]

Real-World Data on BIC/FTC/TAF Use in Pediatric Patients

In a retrospective, single-center study of 74 pediatric patients receiving BIC/FTC/TAF 50/200/25 mg, 83.8% of patients were virologically suppressed at the last study visit. Twenty-eight patients experienced VF, and 16 (57.1%) of those patients achieved virologic suppression by last visit with multifaceted interventions to improve adherence. One patient discontinued BIC/FTC/TAF due to a suspected AE, and 1 patient switched to a different ART regimen.[9]

# Product Labeling[1]

## Dosage and Administration

### Recommended dosage in adults and pediatric patients weighing ≥25 kg

The recommended dosage of BIC/FTC/TAF is one tablet containing 50 mg of BIC, 200 mg of FTC, and 25 mg of TAF taken orally once daily with or without food in adults and pediatric patients weighing ≥25 kg with an estimated CrCl ≥30 mL/min.

### Recommended dosage in pediatric patients weighing ≥14 kg to <25 kg

The recommended dosage of BIC/FTC/TAF is one tablet containing 30 mg of BIC, 120 mg of FTC, and 15 mg of TAF taken orally once daily with or without food in pediatric patients weighing ≥14 kg to <25 kg with an estimated CrCl ≥30 mL/min. For children unable to swallow a whole tablet, the tablet can be split and each part taken separately as long as all parts are ingested within approximately 10 minutes.

## Use in Specific Populations

### Pediatric use

The safety and effectiveness of BIC/FTC/TAF have been established as a complete regimen for the treatment of HIV-1 infection in pediatric patients weighing ≥14 kg who have no ARV treatment history; or or with an ARV treatment history and not virologically suppressed, with no known or suspected substitutions associated with resistance to the INSTI class, FTC, or TFV; or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA <50 c/mL) on a stable ARV regimen with no known or suspected resistance to BIC or TFV.

Use of BIC/FTC/TAF in pediatric patients weighing ≥14 kg is supported by the following:

- Trials in adults
- An open-label trial in three age-based cohorts of virologically suppressed pediatric subjects:
  - Cohort 1: 12 to <18 years of age and weighing ≥35 kg receiving BIC/FTC/TAF through Week 48 (N=50),

- Cohort 2: 6 to <12 years of age and weighing ≥25 kg receiving BIC/FTC/TAF through Week 24 (N=50), and
- Cohort 3: >2 years of age and weighing ≥14 kg to <25 kg through Week 24 (N=22). No pediatric subjects 2 years of age were enrolled; of the 6 pediatric subjects who were 3 years of age at enrollment, 3 subjects weighed between 14 to <15 kg.

The safety and efficacy of BIC/FTC/TAF in these pediatric subjects were similar to that in adults, and there was no clinically significant change in exposure for the components of BIC/FTC/TAF.

Safety and effectiveness of BIC/FTC/TAF in pediatric patients weighing <14 kg have not been established.

# Clinical Data on BIC/FTC/TAF Use in Pediatric Participants

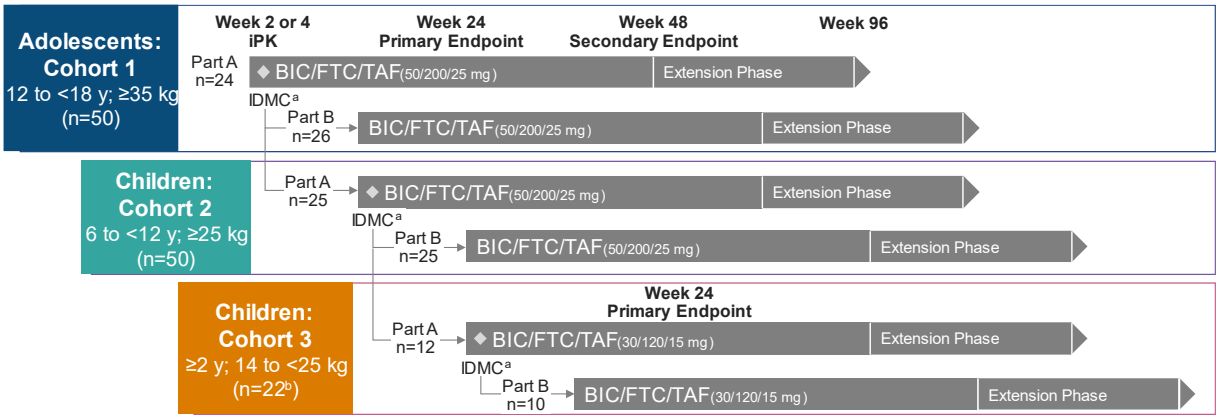
## Study GS-US-380-1474

### Study design and demographics[2]

Study 1474 was a phase 2/3, single-arm, multicenter, multicohort, two-part, open-label clinical trial that evaluated the PK, safety, tolerability, and efficacy of BIC/FTC/TAF 50/200/25 mg STR in virologically suppressed adolescents aged 12 to <18 years (Cohort 1; n=50) and children aged 6 to <12 years (Cohort 2; n=50) with HIV-1. Participants from Cohorts 1 and 2 were enrolled in two groups: Part A (Cohort 1, n=24 and Cohort 2, n=25) assessed PK and confirmed dosing of BIC/FTC/TAF, and Part B assessed the safety and efficacy of BIC/FTC/TAF (Figure 1). Cohort 3 consisted of children with HIV-1 aged ≥2 years who weighed between 14 to <25 kg. This cohort was treated with a BIC/FTC/TAF 30/120/15 mg STR (60% of full strength).

Participants were switched from their current, stable ARV regimen of two NRTIs plus a third agent to BIC/FTC/TAF. Key inclusion criteria were weight ≥35 kg (for adolescents) or ≥25 kg (for children), HIV-1 RNA <50 c/mL for ≥6 months prior to screening, CD4 count ≥200 cells/mcL, and $eGFR_{Schwartz}$ ≥90 mL/min/1.73 $m^2$. The primary objectives were an assessment of PK parameters ($AUC_T$ and $C_T$) of BIC at steady state at Weeks 2 and 4 (Cohorts 1 and 2) and safety and tolerability of BIC/FTC/TAF through Week 24. Secondary objectives included assessment of the safety and tolerability of BIC/FTC/TAF through Week 48, the proportion of participants with HIV-1 RNA <50 c/mL by FDA Snapshot analysis at Weeks 24 and 48, assessment of PK parameters ($C_{max}$ and $T_{max}$ for BIC and $AUC_T$, $C_{max}$, and $C_T$ for FTC and TAF), and the change from baseline and percentage change in CD4 counts at Weeks 24 and 48.

**Figure 1. Study 1474: Study Design[2]**




Abbreviations: IDMC=Independent Data Monitoring Committee; iPK=intensive PK monitoring.
[a]IDMC reviewed data once 50% of participants reached Week 12 and once all participants completed the iPK visit (Week 2 or 4).
[b]Six participants switched treatment to adult-strength BIC/FTC/TAF once they weighed >25 kg.

**Table 1. Study 1474: Baseline Demographics and Disease Characteristics[2,4]**

| Key Demographics and Characteristics | Cohort 1: Adolescents (n=50) | Cohort 2: Children 6 to <12 Years (n=50) | Cohort 3: Children ≥2 Years (n=22) |
|---|---|---|---|
| Age, median (range), years | 15 (12–17) | 10 (6–11) | 6 (3–7)[a] |
| Weight, median (IQR), kg | 44.8 (40–56.1) | 29 (26.9–32.5) | 18.7 (15.2–21.7) |
| Female, n (%) | 32 (64) | 27 (54) | 11 (50) |
| Race, Black/Asian/White, n (%) | 32 (65)/13 (27)/1 (2) | 36 (72)/11 (22)/2 (4) | 16 (73)/5 (23)/0[b] |
| CD4 count, median (IQR), cells/mcL | 750 (586–926) | 898 (707–1121) | 962 (748–1419) |
| $eGFR_{Schwartz}$, median (IQR), mL/min/1.73 $m^2$ | 145 (134–170) | 153.5 (144–173) | 160.5 (145–168) |
| Vertical transmission, n (%) | 45 (90) | 48 (96) | 22 (100) |

[a]Median (IQR).
[b]Black/Asian race reported; 1 participant had "other" race.

# PK results

### *Cohort 1 (adolescents)[2]*

The BIC $C_T$ in adolescents was 35% lower than what was observed in adults in phase 3 clinical trials. FTC and TAF exposures ($AUC_T$) in adolescents were similar to those observed in adults in phase 3 clinical trials and were within the known safety ranges of historical data in adults and adolescents following administration of approved FTC/TAF-containing products (Table 2).

**Table 2. Study 1474: Summary of PK Parameters for Cohort 1 (Adolescents, Part A)[2]**

| PK Parameter, Mean (CV) | | Cohort 1 Adolescents | BIC/FTC/TAF-Treated Adults[a] | Adolescent/Adult GLSM[b] (90% CI) |
|---|---|---|---|---|
| BIC[c] | n | 50 | 1193 | – |
| | $AUC_T$, h·ng/mL | 89,100 (31) | 102,000 (26.9) | 86.3 (80–93) |
| | $C_{max}$, ng/mL | 6240 (27.1) | 6150 (22.9) | 100 (93.8–107) |
| | $C_T$, ng/mL | 1780 (44.4) | 2610 (35.2) | 65.4 (58.3–73.3) |

| PK Parameter, Mean (CV) | | Cohort 1 Adolescents | BIC/FTC/TAF-Treated Adults[a] | Adolescent/Adult GLSM[b] (90% CI) |
|---|---|---|---|---|
| FTC[d] | n | 24 | 77 | – |
| | $AUC_T$, h·ng/mL | 13,600 (21.7) | 12,300 (29.2) | 113 (102–124) |
| | $C_{max}$, ng/mL | 2690 (34) | 2130 (34.7) | 127 (111–145) |
| | $C_T$, ng/mL | 64.4 (25) | 96 (37.4)[e] | 69.3 (61.6–77.9) |
| TAF[c] | n | 49 | 486 | – |
| | $AUC_T$, h·ng/mL | 196 (50.3) | 142 (17.3) | 128 (116–141) |
| | $C_{max}$, ng/mL | 133 (70.2) | 121 (15.4) | 88.6 (75–105) |

[a]Pooled population PK data from four phase 3 studies in adult PWH.
[b]Reported as ratio of test to reference.
[c]Cohort 1 (adolescent) data were obtained from population PK data.
[d]Cohort 1 (adolescent) data were obtained from the intensive PK substudy (Part A).
[e]n=74.

### *Cohort 2 (children)*[2]

BIC exposures ($AUC_T$ and $C_T$) in children were within the predefined PK boundaries and consistent with the ranges of BIC exposures observed in adults in phase 3 clinical trials of BIC/FTC/TAF, although BIC $C_T$ was 11% lower in children than in adults. Mean FTC and TAF exposures ($AUC_T$) were higher in children than in adults but were within known safety ranges of historical data in adults and children (Table 3).

**Table 3. Study 1474: Summary of PK Parameters for Cohort 2 (Children, Part A)**[2]

| PK Parameter, Mean (CV) | | Cohort 2: Children, Part A | BIC/FTC/TAF-Treated Adults[a] | Children/Adult GLSM[b] (90% CI) |
|---|---|---|---|---|
| BIC[c] | n | 50 | 1193 | – |
| | $AUC_T$, h·ng/mL | 128,000 (27.8) | 102,000 (26.9) | 125 (117–134) |
| | $C_{max}$, ng/mL | 9460 (24.3) | 6150 (22.9) | 153 (143–163) |
| | $C_T$, ng/mL | 2360 (39) | 2610 (35.2) | 88.9 (80.6–98) |
| FTC[d] | n | 25 | 77 | – |
| | $AUC_T$, h·ng/mL | 17,600 (36.9) | 12,300 (29.2) | 143 (127–159) |
| | $C_{max}$, ng/mL | 3890 (31) | 2130 (34.7) | 185 (162–210) |
| | $C_T$, ng/mL | 227 (322.8)[e] | 96 (37.4)[f] | 95 (69.9–129) |
| TAF[c] | n | 47 | 486 | – |
| | $AUC_T$, h·ng/mL | 278 (40.3) | 142 (17.3) | 183 (165–202) |
| | $C_{max}$, ng/mL | 205 (44.6) | 121 (15.4) | 153 (136–173) |

[a]Pooled population PK data from four phase 3 studies in adult PWH.
[b]Reported as ratio of test to reference.
[c]Cohort 2 (children) data were obtained from population PK data.
[d]Cohort 2 (children) data were obtained from the intensive PK substudy (Part A).
[e]n=24.
[f]n=74.

### *Cohort 3 (children ≥2 years)*[4]

Cohort 3 consisted of children aged ≥2 years who weighed between 14 and <25 kg who were treated with BIC/FTC/TAF 30/120/15 mg STR. Intensive PK sampling illustrated that BIC exposures ($AUC_T$ and $C_{max}$) in children who weighed 14 to 25 kg were within the PK equivalence ranges of BIC exposures observed in adults (Table 4). Although $C_T$ in children was lower than that observed in adults, it was still approximately 12-fold greater than the protein-adjusted 95% effective concentration (162 ng/mL) against wild-type HIV-1 virus. Although the 90% CIs for some FTC and TAF exposure parameters fell outside of the equivalence boundaries, exposure parameters in this population were generally consistent with the known efficacy and safety ranges of historical data in adults and children (Table 4).

**Table 4. Study 1474: Summary of PK Parameters for Cohort 3 (Children, Part A)[4]**

| PK Parameter | | Cohort 3 (n=12)[a] | BIC/FTC/TAF-Treated Adults[b] | GLSM Ratio, Children/Adult (90% CI), %[c] |
|---|---|---|---|---|
| BIC, GLSM | $AUC_T$, h·ng/mL | 105,892 | 98,430 | 107.6 (96.7–119.7) |
| | $C_{max}$, ng/mL | 9856.7 | 5986.1 | 164.7 (149.5–181.4) |
| | $C_T$, ng/mL | 1604.8 | 2453 | 65.4 (49.1–87.2) |
| FTC, GLSM | $AUC_T$, h·ng/mL | 14,708.4 | 11,789.5 | 124.8 (111.8–139.2) |
| | $C_{max}$, ng/mL | 3629.6 | 2004 | 181.1 (150.1–218.5) |
| | $C_T$, ng/mL | 74.3 | 89.9 | 82.6 (47.7–143.1) |
| TAF, GLSM | $AUC_T$, h·ng/mL | 281.7 | 194.6 | 144.7 (114.9–182.2) |
| | $C_{max}$, ng/mL | 392.8 | 227.2 | 172.9 (139.8–213.8) |
| | $AUC_{last}$, h·ng/mL | 279.7 | 192.5 | 145.3 (115.3–183.1) |

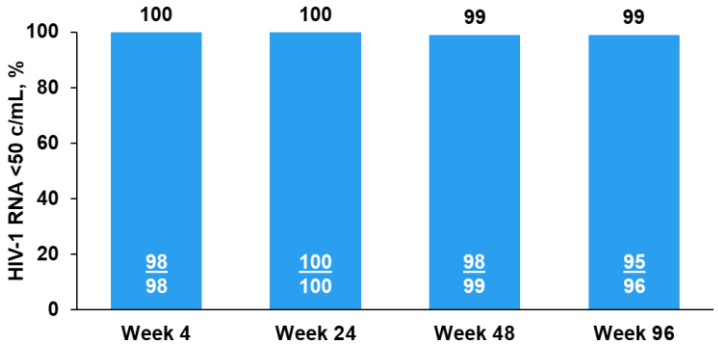
[a]One participant had missing BIC and FTC PK data for $C_T$.
[b]Pooled PK data from four phase 3 studies in adult PWH; n=1193 for BIC and n=74 to 77 for FTC and TAF reference PK data.
[c]PK equivalence was met if the 90% CIs of the GLSM ratio were within the predefined equivalence boundary of 50 to 200%.

## Efficacy and safety results

### *Cohorts 1 and 2: pooled efficacy results through Week 96*

High rates of virologic suppression (HIV-1 RNA <50 c/mL) were maintained with BIC/FTC/TAF through Week 96 with no treatment-emergent resistance (Figure 2).[3] The mean changes from baseline in CD4 count between Weeks 2 and 48 ranged from -40 to +56 cells/mcL. Two participants met the criteria for resistance testing at Week 48, and no emergent resistance was reported. Three participants had a resistance mutation to FTC at baseline and maintained virologic suppression through Week 48.[2]

**Figure 2. Study 1474: Virologic Suppression in Cohorts 1 and 2 Through Week 96 (M=E Analysis)[3]**




### *Cohorts 1 and 2: pooled safety results through Week 96*

Of the 100 participants included in this analysis, 86% experienced AEs of any grade (Table 5). AEs deemed study drug-related by investigators and occurring in >1 participant included abdominal discomfort (n=3) and transient neutropenia (n=2).[3] One 7-year-old female participant with a past medical history of anxiety and neuropsychiatric changes experienced Grade 2 insomnia and anxiety at Week 20; this was considered to be treatment-related by the investigator, and the participant discontinued the study.[2] Thirty participants experienced treatment-emergent Grade 3 or 4 laboratory abnormalities,

with the most frequent being hematuria (16%). Between Weeks 1 and 96, the median change in $eGFR_{Schwartz}$ was -15.5 mL/min/1.73 $m^2$.[3]

**Table 5. Study 1474: Safety Outcomes at Week 96 (Cohorts 1 and 2)[3]**

| | | Cohorts 1 and 2 (n=100) |
|---|---|---|
| Exposure to study drug, median (IQR), weeks | | 151.4 (125.6–153.5) |
| Any AE, n (%) | | 86 (86) |
| Any-grade AE in ≥10% in either group, n (%) | URTI | 30 (30) |
| | Cough | 15 (15) |
| | Diarrhea | 11 (11) |
| | Headache | 11 (11) |
| | Nasopharyngitis | 11 (11) |
| | Vomiting | 8 (8) |
| AEs related to study drug, n (%) | | 13 (13) |
| Grade 3–4 AEs, n (%) | | 5 (5) |
| Serious AEs, n (%) | | 5 (5) |
| AEs that led to study drug discontinuation,[a] n (%) | | 1 (1) |
| Death, n | | 0 |

[a]Discontinuation due to Grade 2 insomnia and anxiety in Cohort 2.

From baseline to Week 48, slight changes in height and weight Z-scores were observed (Table 6).[2]

**Table 6. Study 1474: Changes From Baseline in Height and Weight Z-Scores[10a]**

| Median (IQR) | | | Cohort 1: Adolescents (n=50) | Cohort 2: Children (n=50) | Cohorts 1 and 2 (n=100) |
|---|---|---|---|---|---|
| **Height** | Baseline | | -0.97 (-1.62 to -0.41) | -0.67 (-1.27 to 0.01) | -0.8 (-1.47 to -0.14) |
| | Change from baseline | Week 24 | 0.05 (-0.06 to 0.2) | 0.01 (-1.13 to 0.14) | 0.04 (-0.09 to 0.16) |
| | | Week 48 | 0.04 (-0.08 to 0.18) | 0.02 (-0.21 to 0.24) | 0.2 (0.04–1.1) |
| **Weight** | Baseline | | -0.54 (-1.55 to 0.39) | -0.35 (-1.3 to 0.45) | -0.45 (-1.5 to 0.4) |
| | Change from baseline | Week 24 | 0.09 (-0.03 to 0.31) | 0.23 (0.09–0.48) | 0.21 (0–0.43) |
| | | Week 48 | 0.17 (-0.15 to 0.41) | 0.33 (0.11–0.64) | 0.27 (-0.01 to 0.51) |

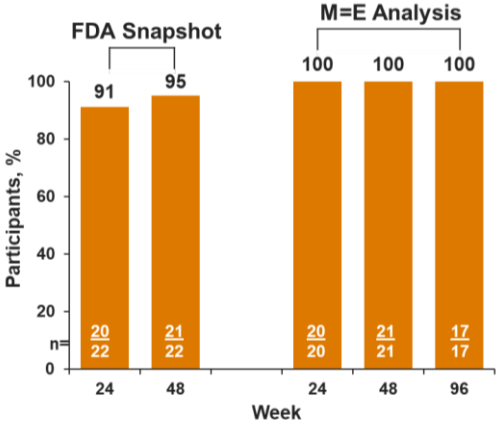
[a]Z-scores generated based on growth charts from year 2000 on the US Centers for Disease Control website.

At Day 1 and Week 4, 100% of participants (100/100) reported that BIC/FTC/TAF was palatable, and its shape and size were acceptable. Median adherence by pill count was 99% through Weeks 24 and 48 and 98% through Week 96.[3]

### *Cohort 3: efficacy results through Week 96[4]*

Virologic suppression (HIV-1 RNA <50 c/mL) was maintained through Week 96 in all participants, as assessed using an M=E analysis (Figure 3), and the median CD4 change from baseline was -137 cells/mcL.

**Figure 3. Study 1474: Virologic Suppression (HIV-1 RNA <50 c/mL) in Cohort 3[4]**




***Cohort 3: safety and tolerability results through Week 48***

As of data cutoff, 11 participants had switched to full-dose BIC/FTC/TAF after reaching a weight of ≥25 kg; these participants were included in the safety analyses. Of the 22 participants included in this analysis, no participants experienced any Grade 3 to 4 AEs or serious AEs, and no participants discontinued the study drug due to an AE.[4]

**Table 7. Study 1474: Safety Outcomes at Week 48 (Cohort 3)[4]**

| Safety Outcome | | Cohort 3 (n=22) |
|---|---|---|
| Study drug exposure duration, median (IQR), weeks | | 99.5 (73.9–108.1) |
| Any AE, n (%) | | 18 (82) |
| Any-grade AE in ≥10%, n (%) | URTI | 7 (32) |
| | Cough | 5 (23) |
| | Diarrhea | 3 (14) |
| | Nasopharyngitis | 3 (14) |
| | Nausea | 3 (14) |
| | Vomiting | 3 (14) |
| AEs related to study drug, n (%) | | 3 (14)[a] |
| Grade 3–4 laboratory abnormalities, n (%) | | 6 (27)[b] |

[a]Neutropenia (n=1); abdominal pain, constipation, and nausea (n=1); irritability, social avoidant behavior, and weight increase (n=1). All AEs related to study drug were Grade 1 or 2.
[b]The only Grade 3 to 4 laboratory abnormality that occurred in >1 participant was decreased neutrophils (n=4); all events of decreased neutrophils were transient.

At Week 96, the median change in $eGFR_{Schwartz}$ was -7.5 mL/min/1.73 $m^2$. Changes in $eGFR_{Schwartz}$ in this cohort were consistent with the known effects of BIC on the renal creatinine transporter. These changes were not considered clinically significant.[11]

Through Week 48, tablet acceptability and palatability were generally high, with ≥79% of those who swallowed the tablets whole reporting them as “easy” or “super easy” to swallow and ≥91% of participants describing the tablets as neutral or positive at palatability assessments. Median adherence by pill count was 99%.[4]

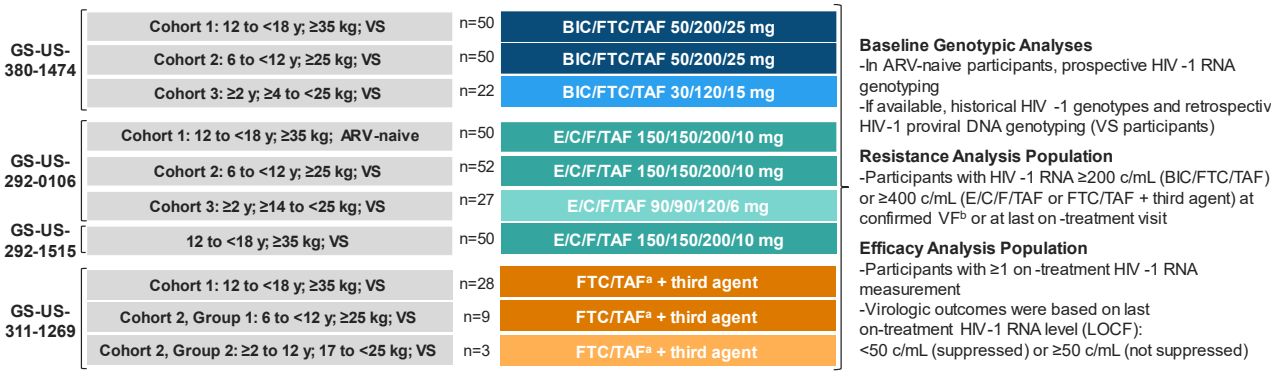
# Pooled Analysis of Resistance to FTC/TAF-Based Regimens in Pediatric Studies

## Study design and demographics[5]

A pooled analysis of four studies (N=341) assessed preexisting drug resistance, treatment-emergent resistance, and the impact of resistance on long-term efficacy of FTC/TAF-based treatment in pediatric populations. Studies included were GS-US-380-1474 (summarized above; BIC/FTC/TAF), GS-US-292-0106 (E/C/F/TAF), GS-US-292-1515 (E/C/F/TAF), and GS-US-311-1269 (FTC/TAF + third agent; Figure 4). Data for BIC/FTC/TAF-treated participants are summarized below.

Participants received an FTC/TAF-based regimen for a median duration of 157 weeks. In the pooled study population, the median (IQR) age was 12 (9–15) years; 52% of participants were aged 12 to <18 years, 42% were aged 6 to <12 years, and 6% were aged 2 to <6 years. Fifty-eight percent of participants were female, 75% were Black, 15% were ARV naive, and 85% were virologically suppressed.

**Figure 4. Pooled Analysis of Resistance: Study Design[5]**




Abbreviation: LOCF=last observation carried forward; VS=virologically suppressed.
[a]In Cohort 1, FTC/TAF was dosed as 200/25 mg if unboosted and 200/10 mg if boosted; in Cohort 2, Group 1, FTC/TAF was dosed as 200/25 mg if boosted or unboosted; in Cohort 2, Group 2, FTC/TAF was dosed as 120/15 mg if boosted or unboosted.
[b]Confirmed VF was defined as HIV-1 RNA ≥50 c/mL at two consecutive study visits or last on-treatment visit.

## Resistance results: participants who received BIC/FTC/TAF[5]

### *Baseline resistance*

Forty-one percent of participants (39/95) who had resistance data at baseline had ≥1 preexisting RAM (Table 8).

**Table 8. Pooled Analysis of Resistance: Baseline Resistance Data in BIC/FTC/TAF-Treated Virologically Suppressed Participants[5,6]**

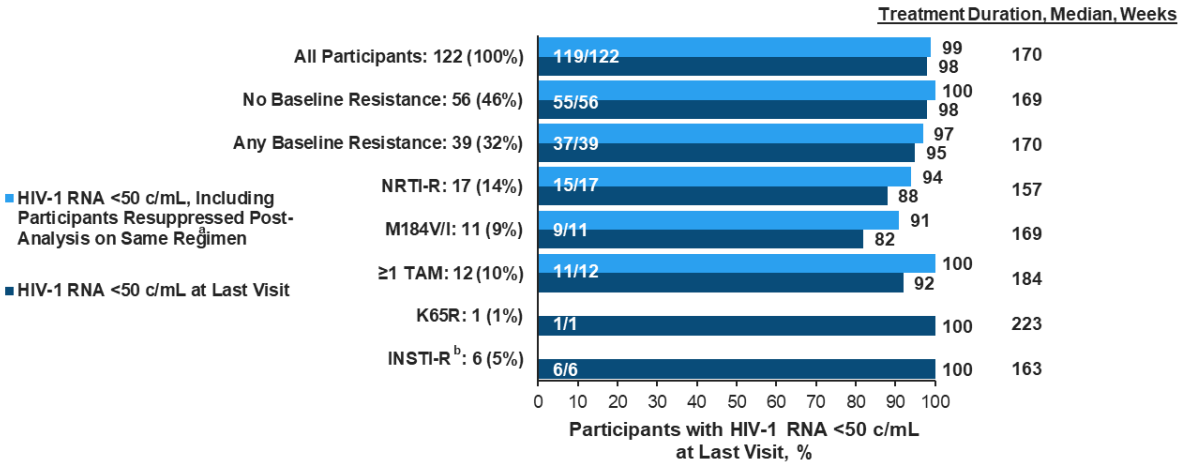
| Participants With Baseline Resistance Data, n/N (%) | BIC/FTC/TAF (n=122) |
|---|---|
| Any baseline resistance[a] | 39/95 (41) |
| NRTI-R | 17/95 (18) |
| M184V/I | 11/95 (12) |
| Any TAM | 12/95 (13) |
| K65R | 1/95 (1)[b] |

| Participants With Baseline Resistance Data, n/N (%) | BIC/FTC/TAF (n=122) |
|---|---|
| NNRTI-R | 28/95 (59) |
| K103N | 6/95 (6) |
| PI-R | 11/95 (11) |
| INSTI-R | 6/92 (7) |
| E92G | 2/92 (2) |
| T97A | 2/92 (2) |
| Y143C | 1/92 (1) |
| R263K | 1/92 (1) |

[a]Those without integrase resistance data were considered as having no INSTI RAM.
[b]This participant maintained virological suppression through Week 223 of BIC/FTC/TAF treatment.

Virologic suppression rates by treatment regimen and baseline resistance showed a durable response; rates for those treated with BIC/FTC/TAF are shown in Figure 5.

**Figure 5. Pooled Analysis of Resistance: Virologic Suppression Among BIC/FTC/TAF-Treated Participants at Last Visit by Baseline Resistance[5]**




[a]This group consisted of participants who were resuppressed on the same ARV regimen and had additional follow-up data after the data cut date, and who completed the study and continued to receive their regimen.
[b]INSTI-R included E92G and T97A (each, n=2); R263K and Y143C (each, n=1).

### *Post-baseline resistance*

Eight of the 122 participants (7%) treated with BIC/FTC/TAF within the resistance analysis population underwent evaluation for the development of resistance. Seven of the 8 participants (88%) were resuppressed without a change in study ARV regimen; no treatment-emergent RAMs were detected.

# Pooled Analysis of Virologically Suppressed Pediatric Participants Who Switched to FTC/TAF-Based Regimens

## Study design and demographics[7]

A pooled analysis of two Gilead studies assessed of the impact of switching to an FTC/TAF-based ARV regimen in virologically suppressed pediatric PWH who were ≥2 years of age and weighed 14 to <25 kg (N=49). All participants had switched from INSTI-, NNRTI, or PI-based ARV regimens within the following studies: GS-US-380-1474 (summarized above; n=22; switched to BIC/FTC/TAF 30/120/15 mg) and GS-US-292-0106 (summarized above; n=27; switched to E/C/F/TAF 90/90/120/6 mg). Outcomes included changes from

baseline to Week 48 in weight, height, BMI, and lipid panel parameters. Data for BIC/FTC/TAF-treated participants are summarized below.

Of the 22 BIC/FTC/TAF-treated participants, the median (IQR) age was 6 (3–7) years; 11 participants were female, 16 were Black, and 5 were Asian. The median (IQR) CD4 count was 962 (748, 1419) cells/mcL, and the median (IQR) CD4% was 32% (29.3–37.2%). All participants were previously treated with an NRTI (ABC, n=18; 3TC, n=17; non–ABC-based, n=5), and 9 were previously treated with efavirenz.

### Results: participants who switched to BIC/FTC/TAF

Weight, height, and BMI Z-scores changed from baseline to Week 48 at rates that were consistent with growth expectations for participant age, and the BMI-for-age percentile increased by 4.2%.[7,8] From baseline to Week 48, percentages of participants who were underweight decreased from 13.6% to 9.1%, respectively, and rates of those with normal weight increased from 63.6% to 68.2%, respectively; rates of those who were overweight or obese remained stable at 22.7% at each time point. In a multivariate linear regression of the entire study population (N=49), being female (*P*=0.0213), and being underweight at baseline (*P*=0.0248) were factors that were associated with a greater change in the BMI-for-age percentile at Week 48.[8]

Among BIC/FTC/TAF-treated participants with lipid panel measurements (n=21), from baseline to Week 48, the percentage of participants of those who had acceptable TC (42.9% to 85.7%, respectively), LDL (47.6% to 76.2%, respectively), and TG (47.6% to 76.2%, respectively) levels increased. The rates of acceptable HDL levels decreased during this time period from 76.2% to 52.4%, respectively. Of the 5 participants who were categorized as overweight or obese at baseline, the following trends in lipid panel measurements were noted at baseline and Week 48: 2 and 0 participants, respectively, had borderline high or high TC; 2 and 2 participants had borderline high or high LDL; 4 and 0 participants had borderline high or high TG; 2 and 4 participants had borderline low or low HDL. Median (IQR) changes from baseline to Week 48 in lipid parameters were as follows: TC, -25 (-46 to -7) mg/dL; LDL, -21 (-43 to -3) mg/dL; TG, -16 (-47 to -1) mg/dL; HDL, -8 (-11 to 1) mg/dL).[8]

# Real-World Data on BIC/FTC/TAF Use in Pediatric Patients

## Retrospective, Single-Center Study in France[9]

### Study design and demographics

A retrospective, single-center study in France was conducted to assess the safety and effectiveness of treatment with BIC/FTC/TAF 50/200/25 mg for ≥6 months in children and adolescents with HIV-1 who weighed ≥25 kg. VF was defined as the inability to attain HIV-1 RNA <50 c/mL within 6 months of BIC/FTC/TAF treatment or the occurrence of virologic rebound (2 consecutive HIV-1 RNA values ≥50 c/mL) among patients who had previously achieved virologic suppression. Genotypic resistance testing was performed for any patient who experienced VF. Among the 74 patients included in the study, the overall median (IQR) age was 11.2 (8.8–15.2) years, 67.6% of all patients were virologically suppressed (HIV-1 RNA <50 c/mL) on ART, 93.2% were ARV experienced (median duration of exposure,

7.2 years), and most (85.1%) had previously been exposed to INSTIs (primarily dolutegravir).

## Results

At a median (IQR) follow-up duration of 40 (21–46) months in the overall population, 62 patients (83.8%) had HIV-1 RNA <50 c/mL without ART changes at their last visit, and 46 patients (62.2%) had sustained virologic suppression. Among the 28 patients who experienced VF, the median (IQR) duration of viremia during treatment with BIC/FTC/TAF was 19 (8–30) months; 16/28 patients (57.1%) who experienced VF achieved HIV-1 RNA <50 c/mL by last visit with multifaceted interventions to improve adherence without changes to ART. Patients with VF, compared with those with sustained virologic suppression, were more likely to have M184V/I mutations at baseline (35.7% vs 12.2%, respectively; *P*=0.04), a lower CD4 cell count (*P*=0.03), and longer follow-up duration during treatment with BIC/FTC/TAF (43 vs 36 months; *P*=0.047). Emergence of an NRTI RAM (T69D/N) occurred in 1 patient who had experienced continuous viremia for 47 months. Two patients discontinued BIC/FTC/TAF treatment during follow-up: 1 patient experienced a suspected AE of gastrointestinal and psychiatric nature that resulted in discontinuation, and 1 patient switched to a different ART regimen.

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# Abbreviations

3TC=lamivudine
ABC=abacavir
AE=adverse event
ART=antiretroviral therapy
ARV=antiretroviral
$AUC_T$=area under the curve over dosing interval
$AUC_{last}$=area under the curve up to the last measurable concentration
BIC=bictegravir
c/mL=copies/mL
CD4=cluster of differentiation 4
$C_{max}$=maximum concentration
$C_T$=trough concentration
CV=coefficient of variation
E/C/F/TAF=elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide
$eGFR_{Schwartz}$=eGFR by Schwartz formula
FTC=emtricitabine
GLSM=geometric least squares mean
INSTI=integrase strand transfer inhibitor
INSTI-R=integrase strand transfer inhibitor resistance
M=E=missing=excluded
NNRTI=non-nucleos(t)ide reverse transcriptase inhibitor
NNRTI-R=non-nucleos(t)ide reverse transcriptase inhibitor resistance
NRTI=nucleos(t)ide reverse transcriptase inhibitor
NRTI-R=nucleos(t)ide reverse transcriptase inhibitor resistance
PI=protease inhibitor
PI-R=protease inhibitor resistance
PK=pharmacokinetic(s)
PWH=people with HIV
RAM=resistance-associated mutation
STR=single-tablet regimen
TAF=tenofovir alafenamide
TAM=thymidine analog mutation
TC=total cholesterol
TFV=tenofovir
TG=triglycerides
$T_{max}$=time to maximum concentration
URTI=upper respiratory tract infection
VF=virologic failure

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