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# Pharmacokinetics (PK), Safety and Efficacy of Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in Virologically Suppressed Pregnant Women With HIV


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# All Author Disclosures

- **Dhananjay Marathe (presenting author)**
  - Gilead Sciences: Employment and restricted stocks

  The potential effects of relevant financial relationship with ineligible company have been mitigated
- **Haeyoung Zhang, Hal Martin, Ludwig Lin, Maggie Davis, Hailin Huang, Deqing Xiao, Priyanka Arora, Ramesh Palaparthy and Sandhya Girish**
  - Gilead Sciences: Employment and restricted stocks

  The potential effects of relevant financial relationship with ineligible company have been mitigated
- **Anchalee Avihingsanon**
  - Gilead Sciences: Speaker honoraria and research grants
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  - ViiV Healthcare: Speaker honoraria and research grants

  The potential effects of relevant financial relationship with ineligible company have been mitigated
- **Ellen Koenig**
  - Gilead Sciences: Study investigator

  The potential effects of relevant financial relationship with ineligible company have been mitigated

# Introduction

- Safe, effective and convenient treatment options are needed for pregnant women with HIV
- B/F/TAF is approved for treatment in people with HIV-1 (PWH)
- Limited data exist on B/F/TAF PK, safety and efficacy during pregnancy

- Bictegravir (BIC) is highly protein bound and metabolized by UGT1A1 and CYP3A4
- Increased activities of CYP3A4 and UGT1A1, along with alterations in protein binding and other physiological changes, have been reported in pregnancy

- To evaluate PK, safety and efficacy of B/F/TAF in pregnancy, a dedicated study was conducted
  - Open-label study (NCT03960645) in 33 pregnant women living with HIV-1
  - All participants were virologically suppressed at study start (HIV-1 RNA < 50 c/mL)

**Primary Objective:**
- Evaluate steady-state PK of BIC and confirm dose of B/F/TAF (50/200/25 mg FDC once daily) in the second and third trimesters of pregnancy

**Secondary Objectives:**
- Evaluate steady-state PK of FTC and TAF
- Assess maintenance of HIV-1 virologic suppression during the second and/or third trimesters of pregnancy

B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BIC, bictegravir; c, copies; CYP3A4, cytochrome P450 3A4; FDC, fixed-dose combination; FTC, emtricitabine; PK, pharmacokinetics; PWH, people with HIV-1; UGT1A1, uridine diphosphate-glucuronosyltransferase 1A1; TAF, tenofovir alafenamide

# Study Design and Sampling Method

**Open-label, single-arm, prospective study of 33 pregnant women with HIV-1 who are VS (VL < 50 c/mL)***

**Treatment with B/F/TAF (up to ~38 weeks)**

## Second and Third Trimester

## 6 and 12 Weeks Postpartum

- Steady-state intensive PK plasma sample collection over 24 hours post-dose (BIC, FTC and TAF)
- Plasma protein binding (BIC and TAF)
- PBMC collection (TFV-DP measurement)†
- Cord blood collection at delivery (BIC and TAF)
- HIV-1 RNA/CD4 cell count
- Safety assessment

## Neonates

- Sparse washout PK samples (BIC and TAF)
- HIV-1 RNA and safety assessment

**GLSM ratios for PK comparisons between pregnancy and postpartum samples**

### 1 Primary Endpoint

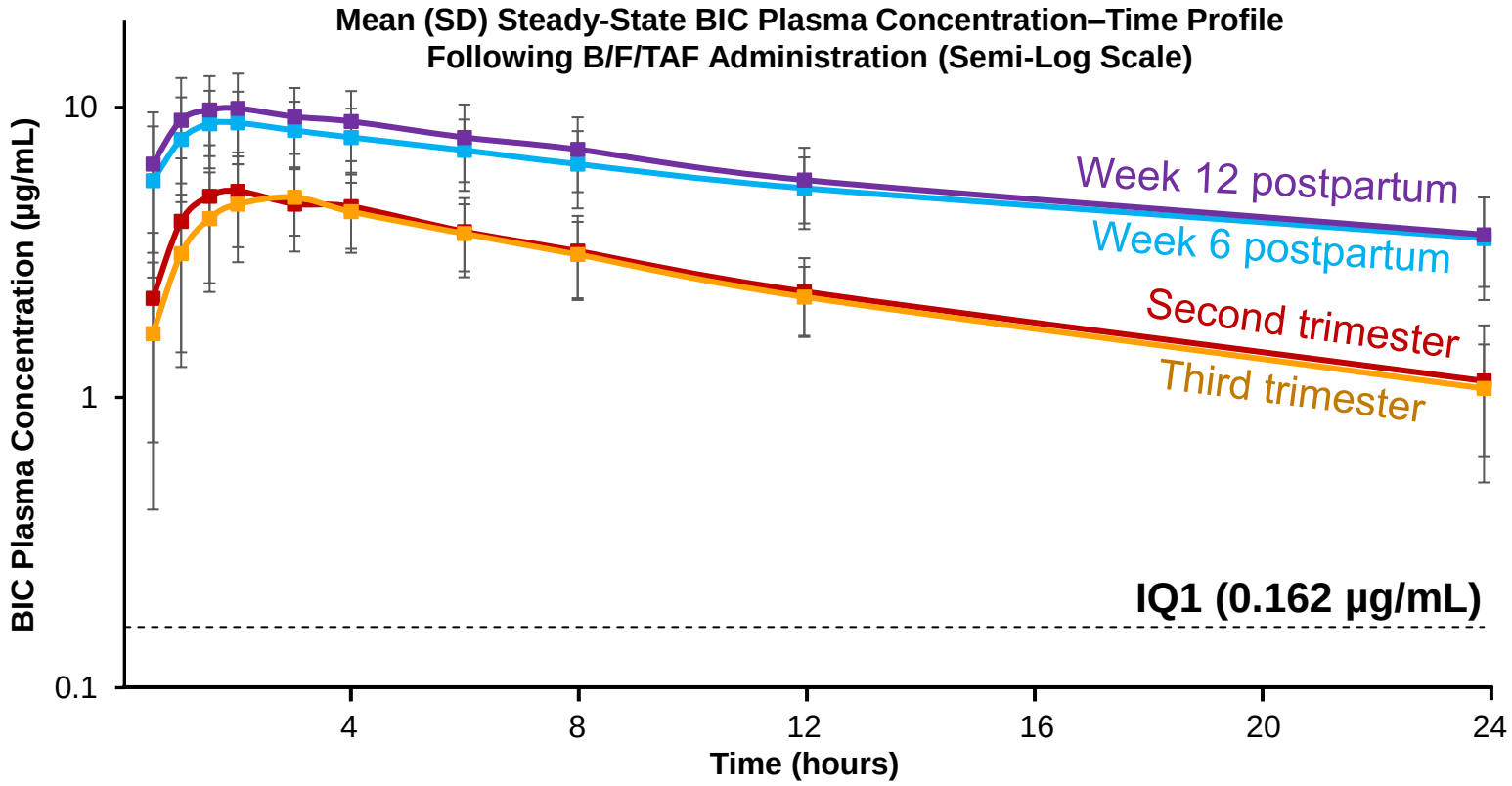
- $AUC_{tau}$ of BIC during second and/or third trimesters through 6 and 12 weeks postpartum

### 2 Secondary Endpoints

- $AUC_{tau}$ for FTC, TAF
- Other PK parameters (e.g., $C_{max}$, $C_{trough}$) for BIC, FTC and TAF
- HIV-1 RNA < 50 c/mL at time of delivery (M = E)

*Study inclusion criteria: aged ≥ 18 to < 40 years, documented VL < 50 c/mL for ≥ 6 months, on stable ART for ≥ 6 months, no documented or suspected resistance to any component of FTC, TFV or INSTIs, GFR ≥ 90 mL/min;
†Exploratory endpoint. ART, antiretroviral therapy; $AUC_{tau}$, area under the plasma drug concentration versus time curve over the dosing interval; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BIC, bictegravir; c, copies; $C_{max}$, maximum observed plasma drug concentration; $C_{trough}$, trough concentration; FTC, emtricitabine; GFR, glomerular filtration rate; GLSM, geometric least-squares mean; INSTI, integrase strand transfer inhibitor; M = E, missing = excluded; PBMC, peripheral blood mononuclear cell; PK, pharmacokinetic; TAF, tenofovir alafenamide; TFV, tenofovir; TFV-DP, tenofovir diphosphate (active metabolite); VL, viral load; VS, virologically suppressed

# Pharmacokinetics of BIC: Plasma Concentration–Time Profiles




- **Concentrations were lower during pregnancy vs. postpartum, but similar within each period (second vs. third trimester; 6 vs. 12 weeks)**
- **Individual $C_{trough}$ values were > IQ1 in all participants across each of the four periods except in one participant* during the second trimester; median $C_{trough}$ was 6.9- and 6.0-fold of IQ1 during the second and third trimesters, respectively**

*Participant on calcium and iron supplements, FTC and TAF exposures in typical population range (> median) at second trimester; the same participant had > 9-fold BIC exposure in third vs. second trimester (i.e., ~ 4.8-fold IQ1).
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BIC, bictegravir; $C_{trough}$, trough concentration; FTC, emtricitabine; IQ1, inhibitory quotient at protein-adjusted 95% effective concentration; SD, standard deviation; TAF, tenofovir alafenamide

# Pharmacokinetics of BIC

| Parameter Mean (%CV) | Second trimester (n = 21) | Third trimester (n = 30) | Week 6 postpartum (n = 31) | Week 12 postpartum (n = 32) | Third trimester vs. Week 12 postpartum (%GLSM ratio [90% CI]) | Pregnancy vs. postpartum (%GLSM ratio) |
|---|---|---|---|---|---|---|
| Total $AUC_{tau}$, h•µg/mL | 62.8 (32.2) | 60.2 (29.1) | 135 (26.9) | 148 (28.5) | 40.6 (36.8, 44.8) | 41.2, 44.7 |
| Unbound $AUC_{tau}$, h•µg/mL | 0.224 (42.0) | 0.219 (33.9) | 0.354 (34.2) | 0.374 (32.2) | 58.8 (52.7, 65.7) | 59.7, 62.4 |
| $C_{max}$, µg/mL | 5.82 (30.1) | 5.37 (25.9) | 9.77 (23.3) | 11.0 (24.9) | 48.2 (43.0, 53.9) | |
| $C_{trough}$, µg/mL | 1.05 (45.2) | 1.07 (41.7) | 3.53 (38.4) | 3.64 (34.1) | 29.0 (25.7, 32.7) | |

- **Compared with 12 weeks postpartum, total and unbound BIC $AUC_{tau}$ during the third trimester were lower by ~59% and ~41%, respectively**
- **In concordance with the current study data, IMPAACT data presented at CROI 2023 showed that total BIC exposure was lower in pregnancy vs. postpartum, while all BIC $C_{trough}$ values were > IQ1[1]**

%CV, percentage coefficient of variation; $AUC_{tau}$, area under the plasma drug concentration versus time curve over the dosing interval; BIC, bictegravir; $C_{max}$, maximum observed plasma concentration of drug; $C_{trough}$, trough concentration; GLSM, geometric least-squares mean; IQ1, inhibitory quotient at protein-adjusted 95% effective concentration

1. Powis KM, et al. CROI 2023, Poster 783. Pharmacokinetics And Virologic Outcomes Of Bictegravir In Pregnancy And Postpartum - CROI Conference (accessed June 22, 2023)

# Pharmacokinetics of BIC

| **Parameter** Mean (%CV) | Second trimester (n = 21) | **Third trimester (n = 30)** | Week 6 postpartum (n = 31) | **Week 12 postpartum (n = 32)** | **Non-pregnant adult PWH (n = 1193)[1,2]** |
|---|---|---|---|---|---|
| **Total $AUC_{tau}$**, h•µg/mL | 62.8 (32.2) | 60.2 (29.1) | 135 (26.9) | 148 (28.5) | 102 (26.9) |
| **Unbound $AUC_{tau}$**, h•µg/mL | 0.224 (42.0) | 0.219 (33.9) | 0.354 (34.2) | 0.374 (32.2) | – |
| $C_{max}$, µg/mL | 5.82 (30.1) | 5.37 (25.9) | 9.77 (23.3) | 11.0 (24.9) | 6.15 (22.9) |
| $C_{trough}$, µg/mL | 1.05 (45.2) | 1.07 (41.7) | 3.53 (38.4) | 3.64 (34.1) | 2.61 (35.2) |

- **Exposure levels in pregnancy are closer to those in non-pregnant adults**
  - **Mean total BIC $AUC_{tau}$ in the third trimester was ~41% lower than values reported in non-pregnant adult PWH[1]**

%CV, percentage coefficient of variation; $AUC_{tau}$, area under the plasma drug concentration versus time curve over the dosing interval; BIC, bictegravir; $C_{max}$, maximum observed plasma concentration of drug; $C_{trough}$, trough concentration; IQ1, inhibitory quotient at protein-adjusted 95% effective concentration; PWH, people with HIV-1.

1. Biktarvy USPI. https://www.gilead.com/-/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi.pdf (accessed June 13, 2023);
2. FDA Biktarvy Uni-Review. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/210251Orig1s000MultidisciplineR.pdf (accessed June 22, 2023)

# Pharmacokinetics of FTC and TAF

- Plasma FTC exposures were lower during pregnancy compared with postpartum; %GLSM ratio for $AUC_{tau}$ ranged from 64.3% to 69.2%
- Plasma TAF exposures were lower during pregnancy compared with postpartum; %GLSM ratio for total $AUC_{tau}$ ranged from 56.5% to 77.6%
  - When adjusted for changes in protein binding, %GLSM ratio for unbound $AUC_{tau}$ ranged from 83.6% to 89.3%
- Trough TFV-DP levels in PBMCs were generally similar (but variable) during pregnancy and postpartum period
- In other published literature, there were changes of similar magnitude in FTC and TAF exposure during pregnancy, and these were not associated with virologic failure or perinatal (vertical) transmission[1,2]
- U.S. DHHS clinical guidelines state that no dose adjustments are required for FTC or TAF during pregnancy[3]

$AUC_{tau}$, area under the plasma drug concentration versus time curve over the dosing interval; DHHS, Department of Health and Human Services; FTC, emtricitabine; GLSM, geometric least-squares mean; PBMC, peripheral blood mononuclear cell; TAF, tenofovir alafenamide; TFV-DP, tenofovir diphosphate

1.Colbers APH, et al. AIDS 2013;27:739-748; 2. Brooks KM, et al. AIDS 2021;35:407-417; 3. DHHS. https://clinicalinfo.hiv.gov/en/guidelines/perinatal/whats-new (accessed June 13, 2023)

# Neonatal PK for BIC

## BIC

- Mean (%CV) cord blood to maternal blood plasma concentration ratio (n = 29): **1.4 (35%)**
- Median $t_{½}$ in neonates (n = 10): **43.1 hours**
- Other neonatal BIC PK parameters were not calculable or meaningful



BIC $t_{½}$ **in neonates** (43 hours) was longer than that in adults (~18 hours across postpartum)

%CV, percentage coefficient of variation; BIC, bictegravir; PK, pharmacokinetic(s); $t_{1/2}$, terminal elimination half-life

# All Participants Were Virologically Suppressed at Delivery and Up to 18 Weeks Postpartum

## Virologic Suppression in Adults

- **Virologic suppression was maintained during pregnancy, delivery and through Week 18 postpartum**
- **All (100%) adult participants had HIV-1 RNA < 50 c/mL at delivery (32/32) and through Week 18 postpartum (32/32)***
- **No virologic failure or treatment-emergent resistance was observed**

## CD4 Cell Count and CD4% in Adults

- CD4 cell count at baseline median (Q1, Q3): **558 (409, 720) cells/μL**
- Change from baseline to Week 12 postpartum, median (Q1, Q3): **159 (27, 296) cells/μL**

- CD4% at baseline, median (Q1, Q3): **32.3% (27.0%, 40.2%)**
- Change from baseline at Week 12 postpartum, median (Q1, Q3): **0.1% (-2.3%, 4.2%)**

## No Virologic Findings in Neonates

- **Neonate participant data available for:**
  - **n = 2 at birth**
  - **n = 3 at 4–8 weeks post birth**
- **All 3 had HIV-1 RNA < 50 c/mL, indicating no perinatal (vertical) HIV-1 transmission**

**In concordance with the current study data efficacy, IMPAACT data presented at CROI 2023 reported that 90% of participants receiving B/F/TAF during pregnancy were virologically suppressed at delivery†[1]**

*Prespecified efficacy analysis using M = E; †Only one participant had a viral load > 200 c/mL
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; c, copies; M = E, missing = excluded; Q, quartile
1. Powis KM, et al. CROI 2023, Poster 783

# B/F/TAF Was Generally Well Tolerated in Adults and Neonates

| | Maternal (N = 33) | Neonate (N = 29) |
|---|---|---|
| **Type of AE n (%)** | | |
| Any AE | 26 (79) | 12 (41) |
| Common AEs | Back pain 4 (12)<br>Gestational diabetes 4 (12)<br>Anemia 3 (9)<br>False labor 3 (9)<br>Preeclampsia 3 (9) | Neonatal jaundice 3 (10)<br>Respiratory distress 3 (10) |
| Drug-related AE | 1 (3)* | 0 |
| SAE | 6 (18) | 5 (17) |
| Drug-related SAE | 1 (3)* | 0 |
| AE leading to premature discontinuation | 0 | 0 |
| Death | 0 | 0 |
| **Laboratory evaluations** | | |
| Grade 1/2<br>Grade ≥ 3 | 24 (72)<br>6 (18) | 5 (17)<br>0 |

All laboratory-related AEs were Grade 1

Majority of AEs were Grade 1/2; Grade ≥ 3 AE reported in 1 (3%) neonate (neonatal asphyxia)

Majority were Grade 1/2; Grade ≥ 3 reported in 2 (6%) participants (gestational diabetes and pyrexia)

One drug-related AE (false labor) was reported; this was an SAE

Grade 3 laboratory AEs of hematuria (5 [15%]) and glycosuria (1 [3%])†

**There were no discontinuations due to AEs**

Median duration of B/F/TAF exposure was 27 weeks
*False labor; †Grade 3 glycosuria in a hyperglycemic participant with gestational diabetes
AE, adverse event; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; SAE, serious adverse event

# Conclusions

- BIC exposure was lower during pregnancy than postpartum; extent of the difference was less pronounced for unbound exposures and in non-pregnant adult PWH[1]
- Overall, individual $C_{trough}$ values were > IQ1 in all participants across each of the four periods (except in one participant during the second trimester)
  - Median $C_{trough}$ was ~7- and 6-fold higher than IQ1 in the second and third trimesters, respectively
- FTC and TAF PK observations were consistent with published literature[2,3]

- All (32/32) adult participants had HIV-1 RNA < 50 c/mL at delivery and maintained virologic suppression through 18 weeks postpartum, with no observed virologic failure or treatment-emergent resistance
- Median CD4 cell count and CD4% remained stable for adult participants through 12 weeks postpartum
- BIC levels in neonates (n = 10) and cord blood data (n = 29) indicated that it crosses the placental barrier
- Data from available neonates (n = 3) did not show any perinatal HIV-1 transmission

- B/F/TAF was well tolerated in pregnant women through their second and third trimesters and postpartum
- No discontinuations due to AEs
- AEs were mostly Grade 1/2; overall incidence and types of AE were consistent with those expected

**Data from this study and available evidence suggest the suitability of once-daily B/F/TAF use throughout pregnancy, including the second and third trimesters, and indicate that no dose change is needed[2-5]**

AE, adverse event; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BIC, bictegravir; c, copies; $C_{trough}$, trough concentration; IQ1, inhibitory quotient at protein-adjusted 95% effective concentration; PWH, people with HIV-1

1. Biktarvy USPI. https://www.gilead.com/-/media/files/pdfs/medicines/hiv/biktarvy/biktarvy_pi.pdf (accessed June 13, 2023); 2.Colbers APH, et al. AIDS 2013;27:739-748; 3. Brooks KM, et al. AIDS 2021;35:407-417;
4. DHHS. https://clinicalinfo.hiv.gov/en/guidelines/perinatal/whats-new (accessed June 13, 2023); 5. Powis KM, et al. CROI 2023, Poster 783

# Acknowledgments

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## Thank you to the investigators, study staff and all participants


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# Pharmacokinetics, Safety and Efficacy of Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in Virologically Suppressed Pregnant Women With HIV

## Supplementary Materials

**Haeyoung Zhang,[1] Hal Martin,[1] Ludwig Lin,[1] Maggie Davis,[1] Hailin Huang,[1] Deqing Xiao,[1]**
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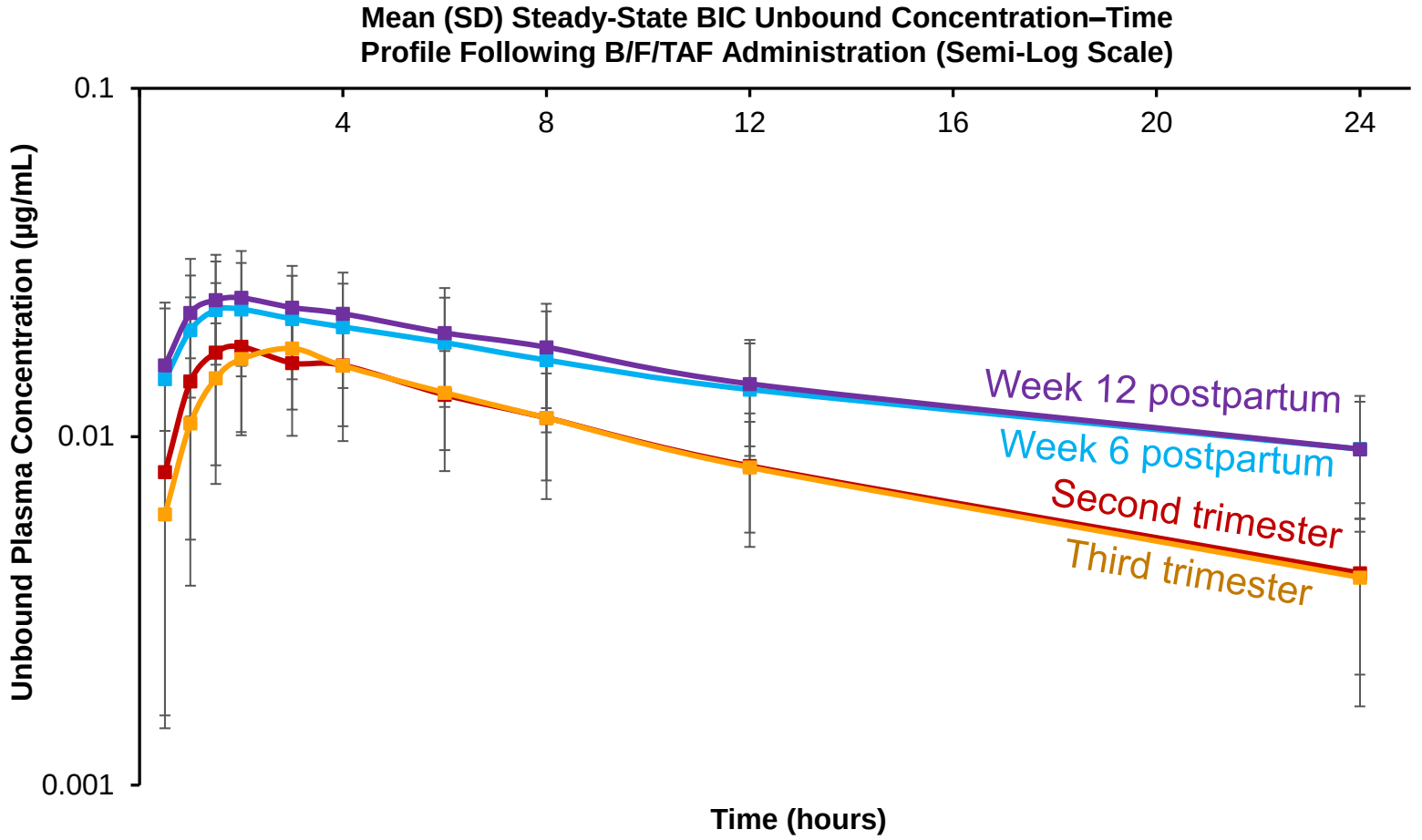
# Demographic and Baseline Characteristics

| Adult participants | N = 33 |
|---|---|
| Age, years, median (Q1, Q3) | 30 (26, 34) |
| Race, n (%)<br>Asian / Black / White / Other | <br>25 (76) / 6 (18) / 1 (3) / 1 (3) |
| Ethnicity, n (%)<br>Hispanic or Latinx | <br>4 (12) |
| HIV-1 RNA < 50 c/mL, n (%) | 33 (100) |
| CD4 count, cells/µL, median (Q1, Q3) | 558 (409, 720) |
| CD4, %, median (Q1, Q3) | 32 (27, 40) |
| **Neonate participants** | **N = 29** |
| Female sex at birth, n (%) | 10 (35) |
| Race, n (%)<br>Asian / Black / Other | <br>24 (83) / 4 (14) / 1 (3) |
| Ethnicity, n (%)<br>Hispanic or Latinx | <br>4 (14) |
| HIV-1 RNA, n (%)<br>< 50 c/mL<br>Missing | <br>2 (7)<br>27 (93) |
| Apgar score, median (Q1 Q3)* | 9 (9, 10) |

*Used to assess status of newborn infants using five measures (appearance of skin color, pulse, grimace response, activity and respiration) on a scale of 0 to 2 for each measure with 10 being the maximum overall Apgar score
c, copies; Q, quartile

# Pharmacokinetics of BIC: Unbound Plasma Concentration–Time Profiles




**Plasma unbound BIC concentrations were lower during pregnancy vs. postpartum, but similar within each period (second vs. third trimester; 6 vs. 12 weeks)**

B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BIC, bictegravir; standard deviation

# Pharmacokinetics of FTC

| Parameter | Second trimester (n = 21) | Third trimester (n = 30) | Week 6 postpartum (n = 31) | Week 12 postpartum (n = 32) | 3rd trimester vs. 12 weeks postpartum (%GLSM ratio [90% CI]) |
|---|---|---|---|---|---|
| **Total $AUC_{tau}$**, h•µg/mL, mean (%CV) | 10.3 (20.0) | 10.4 (20.3) | 16.3 (24.7) | 15.3 (21.9) | 69.2 (65.9, 72.7) |
| $C_{max}$, µg/mL, mean (%CV) | 2.64 (36.6) | 2.59 (26.5) | 3.39 (28.0) | 3.36 (26.9) | 77.5 (70.3, 85.3) |
| $C_{trough}$, µg/mL, mean (%CV) | 0.0598 (104) | 0.0514 (27.2) | 0.152 (179) | 0.0811 (33.7) | 64.7 (59.3, 70.6) |
| $T_{max}$, h, median (Q1, Q3) | 1.50 (1.00, 2.00) | 1.50 (1.00, 2.00) | 1.50 (1.00, 1.55) | 1.00 (1.00, 1.75) | – |
| $t_{½}$, h, median (Q1, Q3) | 6.43 (5.62, 6.70) | 6.41 (5.59, 6.90) | 6.27 (5.65, 6.76) | 5.76 (5.29, 6.58) | – |

**FTC exposures were lower during pregnancy compared with postpartum**

%CV, percentage coefficient of variation; $AUC_{tau}$, area under the plasma drug concentration versus time curve over the dosing interval; CI, confidence interval; $C_{max}$, maximum observed plasma concentration of drug; $C_{trough}$, trough concentration; FTC, emtricitabine; GLSM, geometric least-squares mean; Q, quartile; $t_{½}$, terminal elimination half-life; $T_{max}$, observed time point of $C_{max}$

# Pharmacokinetics of TAF

| Parameter | Second trimester (n = 21) | Third trimester (n= 30) | Week 6 postpartum (n = 31) | Week 12 postpartum (n = 32) | 3rd trimester vs. 12 weeks postpartum (%GLSM ratio [90% CI]) |
|---|---|---|---|---|---|
| **Total $AUC_{tau}$**, h•µg/mL, mean (%CV) | 0.236 (45.6) | 0.212 (45.0) | 0.374 (41.0) | 0.296 (31.8) | 69.7 (58.6, 82.9) |
| **Unbound $AUC_{tau}$**, h•µg/mL, mean (%CV) | 0.015 (28.2) | 0.016 (28.4) | 0.018 (33.8) | 0.017 (23.4) | 89.2 (78.2, 102) |
| $C_{max}$, µg/mL, mean (%CV) | 0.332 (52.1) | 0.271 (42.1) | 0.506 (49.2) | 0.495 (52.5) | 57.1 (46.0, 70.9) |
| $C_{last}$, µg/mL, mean (%CV) | 0.00449 (114) | 0.00480 (84.4) | 0.00313 (59.1) | 0.00336 (59.5) | – |
| $T_{max}$, h, median (Q1, Q3) | 0.75 (0.50, 1.50) | 1.00 (0.75, 1.50) | 0.75 (0.50, 1.00) | 0.75 (0.50, 1.00) | – |
| $t_{½}$, h, median (Q1, Q3) | 0.30 (0.25, 0.46) | 0.28 (0.22, 0.35) | 0.40 (0.35, 0.51) | 0.35 (0.30, 0.43) | – |

**TAF exposures were lower during pregnancy compared with postpartum**

%CV, percentage coefficient of variation; $AUC_{tau}$, area under the plasma drug concentration versus time curve over the dosing interval; CI, confidence interval; $C_{last}$, last observed quantifiable concentration of the drug; $C_{max}$, maximum observed plasma concentration of drug; GLSM, geometric least-squares mean; TAF, tenofovir alafenamide; $t_{½}$, terminal elimination half-life; $T_{max}$, observed time point of $C_{max}$

# Percentage GLSM Ratios of $AUC_{tau}$ for B/F/TAF

| | BIC | | FTC | TAF | |
|---|---|---|---|---|---|
| | $AUC_{tau}$ | Unbound $AUC_{tau}$* | $AUC_{tau}$ | $AUC_{tau}$ | Unbound $AUC_{tau}$* |
| **Second trimester vs. 6 weeks postpartum** | n = 20/31 | | n = 21/31 | n = 15/27 | |
| | 44.7 (40.0, 49.8) | 61.8 (55.3, 69.0) | 64.3 (61.0, 67.8) | 62.5 (50.8, 77.0) | 83.6 (72.9, 95.9) |
| **Second trimester vs. 12 weeks postpartum** | n = 20/32 | | n = 21/32 | n = 15/30 | |
| | 41.2 (36.7, 46.3) | 59.7 (52.5, 68.0) | 67.4 (63.5, 71.6) | 77.6 (65.4, 92.1) | 89.3 (79.0, 100.8) |
| **Third trimester vs. 6 weeks postpartum** | n = 30/31 | | n = 30/31 | n = 17/27 | |
| | 44.4 (40.0, 49.3) | 62.4 (55.7, 69.9) | 65.1 (61.8, 68.6) | 56.5 (46.3, 69.0) | 86.2 (71.9, 103.2) |
| **Third trimester vs. 12 weeks postpartum** | n = 30/32 | | n = 30/32 | n = 17/30 | |
| | 40.6 (36.8, 44.8) | 58.8 (52.7, 65.7) | 69.2 (65.9, 72.7) | 69.7 (58.6, 82.9) | 89.2 (78.2, 101.6) |

**The range of % GLSM ratios for comparing BIC $AUC_{tau}$ during pregnancy vs. postpartum (primary endpoint) was 41% to 45%; the corresponding range for unbound BIC was 59% to 62%**

Values in the table are % GLSM ratios with 90% confidence intervals in parentheses; n = number of participants in the pregnancy (test)/postpartum (reference) analysis set
*Unbound $AUC_{tau}$ = $AUC_{tau}$ × fraction unbound
$AUC_{tau}$, area under the plasma drug concentration versus time curve over the dosing interval; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BIC, bictegravir; FTC, emtricitabine; GLSM, geometric least-squares mean; TAF, tenofovir alafenamide

# Additional Data: Pharmacokinetics of BIC, FTC and TAF

| Parameter | Second trimester (n = 21) | Third trimester (n = 30) | Week 6 postpartum (n = 31) | Week 12 postpartum (n = 32) |
|---|---|---|---|---|
| **BIC** | | | | |
| $CL_{SS}/F$, mL/h, mean (%CV) | 912 (47.5) | 902 (31.8) | 399 (28.4) | 362 (26.5) |
| $V_Z/F$, mL, mean (%CV) | 11,900 (37.1) | 13,400 (32.4) | 10,300 (35.9) | 8,690 (27.6) |
| $T_{max}$, h, median (Q1, Q3) | 2.00 (1.50, 3.00) | 2.00 (1.50, 3.00) | 1.50 (1.00, 3.00) | 1.50 (1.00, 2.00) |
| $t_{½}$, h, median (Q1, Q3) | 9.09 (8.24, 11.5) | 9.91 (9.10, 11.4) | 18.2 (14.4, 21.5) | 17.4 (14.3, 19.4) |
| **FTC** | | | | |
| $CL_{SS}/F$, mL/h, mean (%CV) | 20,200 (19.7) | 20,000 (21.1) | 13,000 (23.9) | 13,600 (20.7) |
| $V_Z/F$, mL, mean (%CV) | 182,000 (20.2) | 185,000 (30.5) | 117,000 (30.1) | 118,000 (28.3) |
| **TAF** | | | | |
| $CL_{SS}/F$, mL/h, mean (%CV) | 123,000 (36.1) | 135,000 (33.2) | 76,900 (37.9) | 92,900 (31.7) |
| $V_Z/F$, mL, mean (%CV) | 62,300 (59.7) | 53,200 (31.4) | 44,400 (30.8) | 49,800 (44.2) |

%CV, percentage coefficient of variation; BIC, bictegravir; $CL_{ss}/F$, apparent oral clearance of the drug at steady state; FTC, emtricitabine; $t_{½}$, terminal elimination half-life; TAF, tenofovir alafenamide; $T_{max}$, observed time point of $C_{max}$; $V_z/F$, apparent volume of distribution

# Neonatal Pharmacokinetics for TAF

## TAF

- Individual cord blood to maternal blood plasma concentration ratios (n = 2): **0.09, 1.12**
- **Other neonatal TAF PK parameters were not calculable due to undetectable TAF in all samples**



**TAF was undetectable in all neonate plasma PK samples**

PK, pharmacokinetic; TAF, tenofovir alafenamide