Clinical trial results:
A Phase 1b, Open-label study to Evaluate the PK, Safety and Efficacy of B/F/TAF in HIV-1 infected, Virologically Suppressed, Pregnant Women in their Second and Third Trimesters

Summary

EudraCT number	2021-001073-23
Trial protocol	Outside EU/EEA
Global end of trial date	18 August 2022

Results information

Result version number	v1
This version publication date	02 March 2023
First version publication date	02 March 2023

Trial information

Trial identification

Sponsor protocol code	GS-US-380-5310

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03960645
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 July 2022
Global end of trial reached?	Yes
Global end of trial date	18 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the steady state pharmacokinetics (PK) of bictegravir (BIC) and confirm the dose of BIC/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg fixed dose combination (FDC) in human immunodeficiency virus 1 (HIV-1) infected, virologically suppressed pregnant women in their second and third trimesters.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 June 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Dominican Republic: 6
Country: Number of subjects enrolled	Thailand: 49
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	62
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	29
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	33
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the Dominican Republic, Thailand, and the United States.

Pre-assignment

Screening details:

33 pregnant women were enrolled in the B/F/TAF group. Neonates born to these women were also enrolled in the study for follow up. A total of 29 neonate participants were enrolled.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	B/F/TAF

Arm description:

Pregnant women participants received fixed dose combination (FDC) tablet of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg, orally, once daily for up to 38 weeks (from the second or third trimesters of pregnancy, depending on enrollment, through 12 weeks post-partum).

Arm type	Experimental
Investigational medicinal product name	B/F/TAF
Investigational medicinal product code	
Other name	GS-9883/F/TAF, Biktarvy®, BVY
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

50/200/25 mg FDC administered as a single dose.

Arm title	Neonates

Arm description:

Neonates born to women participants in the study were followed from birth up to 8 weeks of age after obtaining consent from the parent or legal guardian. None of the neonates participating in the study were treated with the study drug.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	B/F/TAF	Neonates
Started	33	29
Completed	32	29
Not completed	1	0
Protocol Violation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	B/F/TAF
Reporting group description:	
Pregnant women participants received fixed dose combination (FDC) tablet of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg, orally, once daily for up to 38 weeks (from the second or third trimesters of pregnancy, depending on enrollment, through 12 weeks post-partum).	
Reporting group title	Neonates
Reporting group description:	
Neonates born to women participants in the study were followed from birth up to 8 weeks of age after obtaining consent from the parent or legal guardian. None of the neonates participating in the study were treated with the study drug.	

Reporting group values	B/F/TAF	Neonates	Total
Number of subjects	33	29	62
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	30	0	
standard deviation	± 5.0	± 0.0	-
Gender categorical			
Units: Subjects			
Female	33	10	43
Male	0	19	19
Race			
Units: Subjects			
Asian	25	24	49
Black	6	4	10
Other	1	1	2
White	1	0	1
Ethnicity			
Units: Subjects			
Hispanic or Latino	4	4	8
Not Hispanic or Latino	29	25	54

End points

End points reporting groups

Reporting group title	B/F/TAF

Reporting group description:

Pregnant women participants received fixed dose combination (FDC) tablet of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg, orally, once daily for up to 38 weeks (from the second or third trimesters of pregnancy, depending on enrollment, through 12 weeks post-partum).

Reporting group title	Neonates

Reporting group description:

Neonates born to women participants in the study were followed from birth up to 8 weeks of age after obtaining consent from the parent or legal guardian. None of the neonates participating in the study were treated with the study drug.

Primary: Pharmacokinetic (PK) Parameter: AUCtau of Bictegravir (BIC)

End point title	Pharmacokinetic (PK) Parameter: AUCtau of Bictegravir

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration verses time curve over the dosing interval). PK analysis set included all enrolled adult participants who took at least 1 dose of study drug (B/F/TAF), and had at least 1 non-missing concentration value reported by the PK laboratory for the corresponding analytes (BIC, FTC, TAF, and tenofovir diphosphate [TFV-DP]). Participants in the PK analysis set with available data were analysed.

End point type	Primary

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The statistical analysis of this primary endpoint is provided in the attachment.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The neonates did not receive the study drug so they were not analyzed for the primary endpoint.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: hours*nanograms per milliliter (h*ng/mL)				
arithmetic mean (standard deviation)				
Second Trimester (n=20)	62772.2 (± 20242.18)			
Third Trimester (n=30)	60163.4 (± 17482.06)			
Week 6 Post-partum (n=31)	134820.3 (± 36217.30)			
Week 12 Post-partum (n=32)	148251.6 (± 42189.17)			

Attachments (see zip file)	Statistical Analysis/380-5310_Primary_Endpoint_StatsAnalysis.

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUCtau of Emtricitabine (FTC) and Tenofovir Alafenamide (TAF)

End point title	PK Parameter: AUCtau of Emtricitabine (FTC) and Tenofovir Alafenamide (TAF)[3]

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration verses time curve over the dosing interval). Participants in the PK analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: h*ng/mL				
arithmetic mean (standard deviation)				
FTC: Second Trimester (n=21)	10263.8 (± 2054.35)			
FTC: Third Trimester (n=30)	10435.2 (± 2121.87)			
FTC: Week 6 Post-partum (n=31)	16277.5 (± 4023.42)			
FTC: Week 12 Post-partum (n=32)	15308.5 (± 3359.83)			
TAF: Second Trimester (n=15)	235.5 (± 107.36)			
TAF: Third Trimester (n=17)	212.1 (± 95.38)			
TAF: Week 6 Post-partum (n=27)	374.3 (± 153.54)			
TAF: Week 12 Post-partum (n=30)	296.4 (± 94.37)			

Attachments (see zip file)	Statistical Analysis/380-

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUClast of BIC, FTC, and TAF

End point title	PK Parameter: AUClast of BIC, FTC, and TAF[4]

End point description:

AUClast is defined as the concentration of drug from time zero to the last observable concentration. Participants in the PK analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: h*ng/mL				
arithmetic mean (standard deviation)				
BIC: Second Trimester (n=21)	63187.5 (± 19814.99)			
BIC: Third Trimester (n=30)	60145.3 (± 17484.52)			
BIC: Week 6 Post-partum (n=31)	135058.9 (± 36348.21)			
BIC: Week 12 Post-partum (n=32)	148265.3 (± 42201.47)			
FTC: Second Trimester (n=21)	10258.5 (± 2049.53)			
FTC: Third Trimester (n=30)	10434.2 (± 2121.13)			
FTC: Week 6 Post-partum (n=31)	16329.7 (± 4095.44)			
FTC: Week 12 Post-partum (n=32)	15308.5 (± 3359.79)			
TAF: Second Trimester (n=21)	220.4 (± 98.98)			
TAF: Third Trimester (n=30)	202.2 (± 84.98)			
TAF: Week 6 Post-partum (n=31)	356.7 (± 151.27)			
TAF: Week 12 Post-partum (n=32)	294.3 (± 97.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax of BIC, FTC, and TAF

End point title	PK Parameter: Cmax of BIC, FTC, and TAF[5]

End point description:

Cmax is defined as the maximum observed concentration of drug during the dosing interval. Participants in the PK analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: ng/mL				
arithmetic mean (standard deviation)				
BIC: Second Trimester (n=21)	5819.0 (± 1752.29)			
BIC: Third Trimester (n=30)	5374.7 (± 1393.86)			
BIC: Week 6 Post-partum (n=31)	9765.5 (± 2274.93)			
BIC: Week 12 Post-partum (n=32)	11025.3 (± 2747.42)			
FTC: Second Trimester (n=21)	2639.1 (± 965.60)			
FTC: Third Trimester (n=30)	2586.0 (± 686.42)			
FTC: Week 6 Post-partum (n=31)	3394.8 (± 951.83)			
FTC: Week 12 Post-partum (n=32)	3360.0 (± 902.47)			
TAF: Second Trimester (n=21)	332.4 (± 173.29)			
TAF: Third Trimester (n=30)	270.9 (± 113.93)			
TAF: Week 6 Post-partum (n=31)	506.4 (± 249.33)			
TAF: Week 12 Post-partum (n=32)	494.6 (± 259.51)			

Attachments (see zip file)	Statistical Analysis/380-

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Ctau of BIC and FTC

End point title	PK Parameter: Ctau of BIC and FTC[6]

End point description:

Ctau is defined as the observed drug concentration at the end of the dosing interval. Participants in the PK analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: ng/mL				
arithmetic mean (standard deviation)				
BIC: Second Trimester (n=20)	1046.4 (± 472.68)			
BIC: Third Trimester (n=30)	1072.4 (± 447.03)			
BIC: Week 6 Post-partum (n=31)	3530.3 (± 1354.20)			
BIC: Week 12 Post-partum (n=32)	3641.9 (± 1241.64)			
FTC: Second Trimester (n=21)	59.8 (± 62.17)			
FTC: Third Trimester (n=30)	51.4 (± 13.98)			
FTC: Week 6 Post-partum (n=31)	152.1 (± 271.50)			
FTC: Week 12 Post-partum (n=32)	81.1 (± 27.34)			

Attachments (see zip file)	Statistical Analysis/380-

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Clast of BIC, FTC, and TAF

End point title	PK Parameter: Clast of BIC, FTC, and TAF[7]

End point description:

Clast is defined as the last observable concentration of drug. Participants in the PK analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: ng/mL				
arithmetic mean (standard deviation)				
BIC: Second Trimester (n=21)	1141.10 (± 631.431)			
BIC: Third Trimester (n=30)	1075.13 (± 447.847)			
BIC: Week 6 Post-partum (n=31)	3535.48 (± 1371.162)			
BIC: Week 12 Post-partum (n=32)	3641.88 (± 1240.605)			
FTC: Second Trimester (n=21)	75.08 (± 130.792)			
FTC: Third Trimester (n=30)	51.65 (± 14.182)			
FTC: Week 6 Post-partum (n=31)	156.16 (± 292.579)			
FTC: Week 12 Post-partum (n=32)	81.18 (± 27.334)			
TAF: Second Trimester (n=21)	4.49 (± 5.130)			
TAF: Third Trimester (n=30)	4.80 (± 4.048)			
TAF: Week 6 Post-partum (n=31)	3.13 (± 1.849)			
TAF: Week 12 Post-partum (n=32)	3.36 (± 1.999)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Tmax of BIC, FTC, and TAF

End point title	PK Parameter: Tmax of BIC, FTC, and TAF[8]

End point description:

Tmax is defined as the time (observed time point) of Cmax. Participants in the PK analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: hours				
median (full range (min-max))				
BIC: Second Trimester (n=21)	2.00 (1.00 to 12.00)			
BIC: Third Trimester (n=30)	2.00 (1.00 to 6.00)			
BIC: Week 6 Post-partum (n=31)	1.50 (0.50 to 12.00)			
BIC: Week 12 Post-partum (n=32)	1.50 (0.50 to 4.00)			
FTC: Second Trimester (n=21)	1.50 (0.50 to 4.00)			
FTC: Third Trimester (n=30)	1.50 (0.50 to 4.00)			
FTC: Week 6 Post-partum (n=31)	1.50 (0.50 to 4.00)			
FTC: Week 12 Post-partum (n=32)	1.00 (0.50 to 3.00)			
TAF: Second Trimester (n=21)	0.75 (0.25 to 4.00)			
TAF: Third Trimester (n=30)	1.00 (0.25 to 3.00)			
TAF: Week 6 Post-partum (n=31)	0.75 (0.25 to 3.00)			
TAF: Week 12 Post-partum (n=32)	0.75 (0.25 to 3.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: t1/2 of BIC, FTC, and TAF

End point title	PK Parameter: t1/2 of BIC, FTC, and TAF[9]

End point description:

t1/2 is defined as the estimate of the terminal elimination half-life of the drug. Participants in the PK analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: hours				
median (full range (min-max))				
BIC: Second Trimester (n=19)	9.09 (4.75 to 16.04)			
BIC: Third Trimester (n=30)	9.91 (7.53 to 16.24)			
BIC: Week 6 Post-partum (n=29)	18.24 (12.18 to 29.59)			
BIC: Week 12 Post-partum (n=30)	17.27 (4.534 to 26.3)			
FTC: Second Trimester (n=20)	6.43 (4.76 to 7.36)			
FTC: Third Trimester (n=30)	6.41 (4.49 to 7.91)			
FTC: Week 6 Post-partum (n=28)	6.27 (4.47 to 7.80)			
FTC: Week 12 Post-partum (n=32)	5.76 (3.83 to 8.19)			
TAF: Second Trimester (n=14)	0.30 (0.22 to 0.66)			
TAF: Third Trimester (n=16)	0.28 (0.19 to 0.62)			
TAF: Week 6 Post-partum (n=26)	0.40 (0.25 to 0.60)			
TAF: Week 12 Post-partum (n=30)	0.35 (0.25 to 0.60)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: CLss/F of BIC, FTC, and TAF

End point title	PK Parameter: CLss/F of BIC, FTC, and TAF[10]

End point description:

CLss/F is defined as the apparent steady-state oral clearance following administration of the drug. Participants in the PK analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: mL/h				
arithmetic mean (standard deviation)				
BIC: Second Trimester (n=20)	911.78 (± 433.301)			
BIC: Third Trimester (n=30)	902.47 (± 287.285)			
BIC: Week 6 Post-partum (n=31)	399.02 (± 113.214)			
BIC: Week 12 Post-partum (n=32)	362.40 (± 95.856)			
FTC: Second Trimester (n=21)	20228.02 (± 3981.186)			
FTC: Third Trimester (n=30)	19975.85 (± 4223.365)			
FTC: Week 6 Post-partum (n=31)	12991.62 (± 3111.349)			
FTC: Week 12 Post-partum (n=32)	13645.71 (± 2830.897)			
TAF: Second Trimester (n=15)	122677.74 (± 44270.041)			
TAF: Third Trimester (n=17)	135061.19 (± 44876.970)			
TAF: Week 6 Post-partum (n=27)	76939.32 (± 29189.555)			
TAF: Week 12 Post-partum (n=30)	92888.59 (± 29461.550)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Vz/F of BIC, FTC, and TAF

End point title	PK Parameter: Vz/F of BIC, FTC, and TAF[11]

End point description:

Vz/F is defined as the apparent volume of distribution of the drug. Participants in the PK analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: mL				
arithmetic mean (standard deviation)				
BIC: Second Trimester (n=19)	11896.24 (± 4417.149)			
BIC: Third Trimester (n=30)	13406.77 (± 4349.429)			
BIC: Week 6 Post-partum (n=29)	10348.47 (± 3713.380)			
BIC: Week 12 Post-partum (n=30)	8692.59 (± 2398.645)			
FTC: Second Trimester (n=20)	181767.32 (± 36739.344)			
FTC: Third Trimester (n=30)	184791.79 (± 56340.526)			
FTC: Week 6 Post-partum (n=28)	117384.90 (± 35385.941)			
FTC: Week 12 Post-partum (n=32)	117660.87 (± 33240.095)			
TAF: Second Trimester (n=14)	62333.17 (± 37242.307)			
TAF: Third Trimester (n=16)	53230.98 (± 16727.325)			
TAF: Week 6 Post-partum (n=26)	44440.06 (± 13678.515)			
TAF: Week 12 Post-partum (n=30)	49837.70 (± 22019.454)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: λz of BIC, FTC, and TAF

End point title	PK Parameter: λz of BIC, FTC, and TAF[12]

End point description:

λz is defined as the terminal elimination rate constant, estimated by linear regression of the terminal elimination phase of the log plasma concentration of drug versus time curve of the drug. Participants in the PK analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

Intensive PK: Predose, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours postdose in second trimester (Weeks 20-28), third trimester (Weeks 30-38), Week 6 post-partum, and Week 12 post-partum

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The neonates did not receive the study drug so they were not analyzed for the secondary endpoint.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: 1/h				
arithmetic mean (standard deviation)				
BIC: Second Trimester (n=19)	0.077 (± 0.0231)			
BIC: Third Trimester (n=30)	0.068 (± 0.0125)			
BIC: Week 6 Post-partum (n=29)	0.040 (± 0.0098)			
BIC: Week 12 Post-partum (n=30)	0.043 (± 0.0134)			
FTC: Second Trimester (n=20)	0.113 (± 0.0142)			
FTC: Third Trimester (n=30)	0.112 (± 0.0173)			
FTC: Week 6 Post-partum (n=28)	0.114 (± 0.0151)			
FTC: Week 12 Post-partum (n=32)	0.120 (± 0.0209)			
TAF: Second Trimester (n=14)	2.227 (± 0.7128)			
TAF: Third Trimester (n=16)	2.550 (± 0.7519)			
TAF: Week 6 Post-partum (n=26)	1.777 (± 0.4685)			
TAF: Week 12 Post-partum (n=30)	1.954 (± 0.4519)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at the Time of Delivery Using the Missing = Excluded Approach in B/F/TAF Group

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at the Time of Delivery Using the Missing = Excluded Approach in B/F/TAF Group[13]

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at the time of delivery was analysed in B/F/TAF group using missing = excluded approach. In this approach, all missing data were excluded in the computation of the percentages (ie, missing data points were excluded from both the numerator and denominator in the computation). Full analysis set included all adult participants who enrolled into the study and took at least 1 dose of study drug (B/F/TAF). Participants in the full analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

At time of delivery

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This secondary endpoint was planned and analyzed only for the B/F/TAF group.

End point values	B/F/TAF			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: percentage of participants				
number (confidence interval 95%)	100.0 (89.1 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Birth Using the Missing = Excluded Approach in Neonates

End point title	Percentage of Participants With HIV-1 RNA < 50 Copies/mL at Birth Using the Missing = Excluded Approach in Neonates[14]

End point description:

The percentage of participants with HIV-1 RNA < 50 copies/mL at the time of birth was analysed in neonates using missing = excluded approach. In this approach, all missing data were excluded in the computation of the percentages (ie, missing data points were excluded from both the numerator and denominator in the computation). Neonate full analysis set included neonates who were born to women participating in the study and had been enrolled into the study as well. Participants in the neonate full analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

At birth

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This secondary endpoint was planned and analyzed only for the Neonates group.

End point values	Neonates			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: percentage of participants				
number (confidence interval 95%)	100.0 (15.8 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality: From enrollment up to 38 weeks + 30 days for B/F/TAF group.
Adverse Events: First dose date up to 38 weeks + 30 days for B/F/TAF group

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs) are reported only for the adult group as the neonate group did not receive any study treatment. B/F/TAF: Safety analysis set included all adult participants who took at least 1 dose of study drug (B/F/TAF).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	B/F/TAF

Reporting group description:

Pregnant women participants received FDC tablet of B/F/TAF 50/200/25 mg, orally, once daily for up to 38 weeks (from the second or third trimesters of pregnancy, depending on enrollment, through 12 weeks post-partum).

Serious adverse events	B/F/TAF		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 33 (18.18%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Nonreassuring foetal heart rate pattern			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
False labour			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Pre-eclampsia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Preterm premature rupture of membranes			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Covid-19			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	B/F/TAF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 33 (57.58%)		
Cardiac disorders			
Foetal heart rate deceleration abnormality			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Pregnancy, puerperium and perinatal conditions			
Gestational diabetes			

subjects affected / exposed	4 / 33 (12.12%)		
occurrences (all)	4		
Oligohydramnios			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Postpartum haemorrhage			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Pre-eclampsia			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Haemorrhoids			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 33 (12.12%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported