Clinical trial results:
ING200336: A Prospective, Interventional Pharmacokinetic and Safety Study of DTG/ABC/3TC in Pregnant Women

Summary

EudraCT number	2013-003527-11
Trial protocol	ES
Global end of trial date	

Results information

Result version number	v1
This version publication date	10 February 2022
First version publication date	10 February 2022

Trial information

Trial identification

Sponsor protocol code	200336

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02075593
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ViiV Healthcare
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, ViiV Healthcare, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, ViiV Healthcare, 1 8664357343, GSKClinicalSupportHD@gsk.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?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	13 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 October 2018
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the total plasma dolutegravir (DTG) Pharmacokinetic (PK) parameters with the DTG/ abacavir (ABC)/ lamivudine (3TC) fixed dose combination (FDC) during Weeks 18-26, Weeks 30-36 of the third trimester of the pregnancy and 8-12 weeks postpartum; and to further characterize the safety and tolerability of DTG/ABC/3TC FDC when used during pregnancy.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 December 2014
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	Russian Federation: 3
Country: Number of subjects enrolled	Spain: 1
Worldwide total number of subjects	4
EEA total number of subjects	1

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The results presented are based on the primary analysis (and includes data up to a maximum of 292 weeks; data cut-off date: 15-Mar-2021). Additional results will be provided within one year after study completion.

Pre-assignment

Screening details:

This is a single arm open-label study in women who became pregnant while participating in study ING117172 (NCT01910402). In this study 4 pregnant women were enrolled. Participant flow data was collected only in pregnant women (enrolled population/study participants) and not in infants, as infants were not considered as enrolled per study design.

Period 1

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

Arms

Arm title	DTG/ABC/3TC - Mother

Arm description:

Participants (pregnant women) received fixed dose combination (FDC) tablet of dolutegravir (DTG) 50 milligrams (mg), abacavir (ABC) 600 mg and lamivudine (3TC) 300 mg once daily, with or without food.

Arm type	Experimental
Investigational medicinal product name	Dolutegravir/Abacavir/Lamivudine fixed dose combination
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Fixed dose combination of dolutegravir 50 mg, abacavir 600 mg and lamivudine 300 mg tablet was administered once daily, with or without food.

Number of subjects in period 1	DTG/ABC/3TC - Mother
Started	4
Infants born to pregnant women	4
Completed	1
Not completed	3
Consent withdrawn by subject	1
Treatment ongoing at the time of analysis	2

Baseline characteristics

Reporting groups	
Reporting group title	DTG/ABC/3TC - Mother

Reporting group description:

Participants (pregnant women) received fixed dose combination (FDC) tablet of dolutegravir (DTG) 50 milligrams (mg), abacavir (ABC) 600 mg and lamivudine (3TC) 300 mg once daily, with or without food.

Reporting group values	DTG/ABC/3TC - Mother	Total	
Number of subjects	4	4	
Age categorical			
Baseline Characteristics data was collected only in pregnant women (enrolled population/study participants) and not in infants, as infants were not considered as enrolled per study design.			
Units: Subjects			
Adults (18-64 years)	4	4	
Age Continuous			
Baseline Characteristics data was collected only in pregnant women (enrolled population/study participants) and not in infants, as infants were not considered as enrolled per study design.			
Units: years			
arithmetic mean	29.3		
standard deviation	± 5.56	-	
Sex: Female, Male			
Baseline Characteristics data was collected only in pregnant women (enrolled population/study participants) and not in infants, as infants were not considered as enrolled per study design.			
Units: Participants			
Female	4	4	
Male	0	0	
Race/Ethnicity, Customized			
Baseline Characteristics data was collected only in pregnant women (enrolled population/study participants) and not in infants, as infants were not considered as enrolled per study design.			
Units: Subjects			
White/Caucasian/European heritage	4	4	

End points

End points reporting groups

Reporting group title	DTG/ABC/3TC - Mother

Reporting group description:

Participants (pregnant women) received fixed dose combination (FDC) tablet of dolutegravir (DTG) 50 milligrams (mg), abacavir (ABC) 600 mg and lamivudine (3TC) 300 mg once daily, with or without food.

Subject analysis set title	DTG/ABC/3TC - Infant
Subject analysis set type	Safety analysis

Subject analysis set description:

This group consisted of Infants born to pregnant women who received a fixed dose combination tablet of dolutegravir, abacavir and lamivudine during pregnancy.

Primary: Area under the plasma concentration time curve at steady state during a dosing interval (AUC [0-tau]) for dolutegravir

End point title	Area under the plasma concentration time curve at steady state during a dosing interval (AUC [0-tau]) for dolutegravir[1]

End point description:

Blood samples were collected at indicated timepoints for Pharmacokinetic (PK) analysis of dolutegravir at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum. Pharmacokinetic Population consists of all participants in the Safety Population (comprised of all participants (pregnant women) who received at least one dose of study treatment) who had at least 1 non-missing PK assessment

End point type	Primary

End point timeframe:

Pre-dose and at 1, 2, 3, 4, 6, 8, 12, 24 hours post-dose at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum

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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[2]			
Units: Micrograms*hours per milliliter				
geometric mean (confidence interval 95%)				
Trimester 2 (Weeks 18-26 of pregnancy)	55.045 (37.918 to 79.907)			
Trimester 3 (Weeks 30-36 of pregnancy)	42.473 (27.613 to 65.330)			
8-12 Weeks Postpartum	78.917 (53.195 to 117.075)			

Notes:

[2] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Primary: Maximum observed plasma concentration (Cmax) for dolutegravir

End point title	Maximum observed plasma concentration (Cmax) for dolutegravir[3]

End point description:

Blood samples were collected at indicated timepoints for PK analysis of dolutegravir at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum.

End point type	Primary

End point timeframe:

Pre-dose and at 1, 2, 3, 4, 6, 8, 12, 24 hours post-dose at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum

Notes:

[3] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[4]			
Units: Micrograms per milliliter				
geometric mean (confidence interval 95%)				
Trimester 2 (Weeks 18-26 of pregnancy)	4.420 (2.906 to 6.724)			
Trimester 3 (Weeks 30-36 of pregnancy)	3.424 (2.038 to 5.753)			
8-12 Weeks Postpartum	5.578 (3.866 to 8.049)			

Notes:

[4] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Primary: Drug concentration at the end of dosing interval (Ctau) for dolutegravir

End point title	Drug concentration at the end of dosing interval (Ctau) for dolutegravir[5]

End point description:

Blood samples were collected at indicated timepoints for PK analysis of dolutegravir at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum.

End point type	Primary

End point timeframe:

24 hours post dose at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum

Notes:

[5] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[6]			
Units: Nanograms per milliliter				
geometric mean (confidence interval 95%)				
Trimester 2 (Weeks 18-26 of pregnancy)	930.1 (562.0 to 1539.3)			
Trimester 3 (Weeks 30-36 of pregnancy)	657.5 (266.1 to 1624.4)			
8-12 Weeks Postpartum	2154.7 (901.4 to 5150.5)			

Notes:

[6] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Primary: Apparent oral clearance (CL/F) for dolutegravir

End point title	Apparent oral clearance (CL/F) for dolutegravir[7]

End point description:

Blood samples were collected at indicated timepoints for PK analysis of dolutegravir at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum.

End point type	Primary

End point timeframe:

Pre-dose and at 1, 2, 3, 4, 6, 8, 12, 24 hours post-dose at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum

Notes:

[7] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[8]			
Units: Liters per hour				
geometric mean (confidence interval 95%)				
Trimester 2 (Weeks 18-26 of pregnancy)	0.739 (0.484 to 1.130)			
Trimester 3 (Weeks 30-36 of pregnancy)	0.952 (0.559 to 1.620)			
8-12 Weeks Postpartum	0.464 (0.062 to 3.476)			

Notes:

[8] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Primary: Steady state volume of distribution (Vss/F) after extravascular

administration for dolutegravir

End point title	Steady state volume of distribution (Vss/F) after extravascular administration for dolutegravir[9]

End point description:

Blood samples were collected at indicated timepoints for PK analysis of dolutegravir at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum.

End point type	Primary

End point timeframe:

Pre-dose and at 1, 2, 3, 4, 6, 8, 12, 24 hours post-dose at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum

Notes:

[9] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[10]			
Units: Liters				
geometric mean (confidence interval 95%)				
Trimester 2 (Weeks 18-26 of pregnancy)	9.665 (6.651 to 14.044)			
Trimester 3 (Weeks 30-36 of pregnancy)	12.326 (7.878 to 19.285)			
8-12 Weeks Postpartum	6.326 (0.048 to 833.336)			

Notes:

[10] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Primary: Half-life (T1/2) for dolutegravir

End point title	Half-life (T1/2) for dolutegravir[11]

End point description:

Blood samples were collected at indicated timepoints for PK analysis of dolutegravir at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum.

End point type	Primary

End point timeframe:

Pre-dose and at 1, 2, 3, 4, 6, 8, 12, 24 hours post-dose at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum

Notes:

[11] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[12]			
Units: Hours				
arithmetic mean (standard deviation)				
Trimester 2 (Weeks 18-26 of pregnancy)	9.215 (± 1.8968)			
Trimester 3 (Weeks 30-36 of pregnancy)	9.401 (± 3.0322)			
8-12 Weeks Postpartum	9.699 (± 3.0427)			

Notes:

[12] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants (pregnant women) with maximum severity of post-Baseline emergent hematology toxicities: Hemoglobin

End point title	Number of participants (pregnant women) with maximum severity of post-Baseline emergent hematology toxicities: Hemoglobin[13]

End point description:

Blood samples were collected for analysis of hemoglobin. Any abnormality was graded according to Division of Acquired Immunodeficiency Syndrome (DAIDS) toxicity scales from Grade 1 to 4 (1=Mild, 2=Moderate, 3=Severe, 4=Potentially life threatening). Number of participants (pregnant women) with maximum severity of post-Baseline emergent toxicities with respect to hemoglobin has been presented. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment.

End point type	Primary

End point timeframe:

Up to Week 32 of study

Notes:

[13] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[14]			
Units: Participants				
Grade 1	1			
Grade 2	0			
Grade 3	0			
Grade 4	0			

Notes:

[14] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Absolute values of the chemistry parameters: Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST)

End point title	Absolute values of the chemistry parameters: Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST)[15]

End point description:

Blood samples were collected for the analysis of chemistry parameters including ALT and AST. 99999 indicates that standard deviation could not be calculated as a single participant was analyzed. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment. Only those participants (pregnant women) with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

At Baseline (Day 1), Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 and Week 32 of study

Notes:

[15] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[16]			
Units: International units per Liter				
arithmetic mean (standard deviation)				
ALT, Baseline (Day 1), n=4	10.8 (± 5.56)			
ALT, Week 4, n=4	15.3 (± 4.43)			
ALT, Week 8, n=4	19.3 (± 17.21)			
ALT, Week 12, n=4	11.0 (± 3.16)			
ALT, Week 16, n=4	10.8 (± 2.36)			
ALT, Week 20, n=4	10.3 (± 7.27)			
ALT, Week 24, n=1	19.0 (± 99999)			
ALT, Week 32, n=2	28.0 (± 15.56)			
AST, Baseline (Day 1), n=4	14.8 (± 4.19)			
AST, Week 4, n=4	17.3 (± 2.22)			
AST, Week 8, n=4	17.3 (± 6.18)			
AST, Week 12, n=4	15.0 (± 1.83)			
AST, Week 16, n=4	14.8 (± 2.63)			
AST, Week 20, n=4	16.3 (± 3.30)			
AST, Week 24, n=1	20.0 (± 99999)			
AST, Week 32, n=2	24.0 (± 8.49)			

Notes:

[16] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in chemistry parameters: ALT and AST

End point title	Change from Baseline in chemistry parameters: ALT and

End point description:

Blood samples were collected for the analysis of chemistry parameters including ALT and AST. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value.

99999 indicates that standard deviation could not be calculated as a single participant was analyzed. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment. Only those participants (pregnant women) with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

Baseline and at Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 and Week 32 of study

Notes:

[17] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[18]			
Units: International units per Liter				
arithmetic mean (standard deviation)				
ALT, Week 4, n=4	4.5 (± 6.03)			
ALT, Week 8, n=4	8.5 (± 11.79)			
ALT, Week 12, n=4	0.3 (± 3.30)			
ALT, Week 16, n=4	0.0 (± 3.56)			
ALT, Week 20, n=4	-0.5 (± 1.73)			
ALT, Week 24, n=1	0.0 (± 99999)			
ALT, Week 32, n=2	19.5 (± 14.85)			
AST, Week 4, n=4	2.5 (± 4.43)			
AST, Week 8, n=4	2.5 (± 2.38)			
AST, Week 12, n=4	0.3 (± 3.10)			
AST, Week 16, n=4	0.0 (± 3.37)			
AST, Week 20, n=4	1.5 (± 1.29)			
AST, Week 24, n=1	-1.0 (± 99999)			
AST, Week 32, n=2	11.0 (± 8.49)			

Notes:

[18] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Absolute values of the chemistry parameters: Bilirubin and Creatinine

End point title	Absolute values of the chemistry parameters: Bilirubin and Creatinine[19]

End point description:

Blood samples were collected for the analysis of chemistry parameters including Bilirubin and Creatinine. 99999 indicates that standard deviation could not be calculated as a single participant was analyzed. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment. Only those participants (pregnant women) with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

At Baseline (Day 1), Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 and Week 32 of study

Notes:

[19] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[20]			
Units: Micromoles per Liter				
arithmetic mean (standard deviation)				
Bilirubin, Baseline (Day 1), n=4	7.3 (± 3.77)			
Bilirubin, Week 4, n=4	5.0 (± 1.83)			
Bilirubin, Week 8, n=4	5.5 (± 2.65)			
Bilirubin, Week 12, n=4	4.5 (± 1.29)			
Bilirubin, Week 16, n=4	4.5 (± 1.29)			
Bilirubin, Week 20, n=4	4.5 (± 1.29)			
Bilirubin, Week 24, n=1	7.0 (± 99999)			
Bilirubin, Week 32, n=2	6.5 (± 0.71)			
Creatinine, Baseline (Day 1), n=4	57.73 (± 16.661)			
Creatinine, Week 4, n=4	50.50 (± 2.990)			
Creatinine, Week 8, n=4	51.58 (± 3.067)			
Creatinine, Week 12, n=4	50.68 (± 3.293)			
Creatinine, Week 16, n=4	47.45 (± 2.001)			
Creatinine, Week 20, n=4	50.60 (± 6.424)			
Creatinine, Week 24, n=1	63.60 (± 99999)			
Creatinine, Week 32, n=2	68.90 (± 3.677)			

Notes:

[20] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in chemistry parameters: Bilirubin and Creatinine

End point title	Change from Baseline in chemistry parameters: Bilirubin and Creatinine[21]

End point description:

Blood samples were collected for the analysis of chemistry parameters including Bilirubin and Creatinine. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. 99999 indicates that standard deviation could not be calculated as a single participant was analyzed. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment. Only those participants (pregnant women) with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

Baseline and at Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 and Week 32 of study

Notes:

[21] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[22]			
Units: Micromoles per Liter				
arithmetic mean (standard deviation)				
Bilirubin, Week 4, n=4	-2.3 (± 2.06)			
Bilirubin, Week 8, n=4	-1.8 (± 1.26)			
Bilirubin, Week 12, n=4	-2.8 (± 2.99)			
Bilirubin, Week 16, n=4	-2.8 (± 2.99)			
Bilirubin, Week 20, n=4	-2.8 (± 2.99)			
Bilirubin, Week 24, n=1	-5.0 (± 99999)			
Bilirubin, Week 32, n=2	2.0 (± 2.83)			
Creatinine, Week 4, n=4	-7.23 (± 14.014)			
Creatinine, Week 8, n=4	-6.15 (± 16.700)			
Creatinine, Week 12, n=4	-7.05 (± 14.328)			
Creatinine, Week 16, n=4	-10.28 (± 17.453)			
Creatinine, Week 20, n=4	-7.13 (± 11.154)			
Creatinine, Week 24, n=1	-19.10 (± 99999)			
Creatinine, Week 32, n=2	19.10 (± 3.253)			

Notes:

[22] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Absolute values of the hematology parameters: hemoglobin

End point title	Absolute values of the hematology parameters: hemoglobin[23]

End point description:

Blood samples were collected for the analysis of hematology parameters including hemoglobin. 99999 indicates that standard deviation could not be calculated as a single participant was analyzed. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment. Only those participants (pregnant women) with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

At Baseline (Day 1), Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 and Week 32 of study

Notes:

[23] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[24]			
Units: Grams per Liter				
arithmetic mean (standard deviation)				
Baseline (Day 1), n=4	127.8 (± 11.24)			
Week 4, n=4	120.8 (± 7.23)			
Week 8, n=4	113.5 (± 7.05)			
Week 12, n=4	116.5 (± 7.14)			
Week 16, n=4	115.0 (± 4.69)			
Week 20, n=4	115.8 (± 8.30)			
Week 24, n=1	127.0 (± 99999)			
Week 32, n=2	140.5 (± 0.71)			

Notes:

[24] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in hematology parameters: Hemoglobin

End point title	Change from Baseline in hematology parameters:

End point description:

Blood samples were collected for the analysis of hematology parameters including hemoglobin. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. 99999 indicates that standard deviation could not be calculated as a single participant was analyzed. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment. Only those participants (pregnant women) with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

Baseline and at Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 and Week 32 of study

Notes:

[25] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[26]			
Units: Grams per Liter				
arithmetic mean (standard deviation)				
Week 4, n=4	-7.0 (± 10.17)			
Week 8, n=4	-14.3 (± 7.37)			
Week 12, n=4	-11.3 (± 4.92)			
Week 16, n=4	-12.8 (± 6.65)			
Week 20, n=4	-12.0 (± 4.97)			
Week 24, n=1	-14.0 (± 99999)			

Week 32, n=2	14.0 (± 8.49)			

Notes:

[26] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Absolute values of the hematology parameters: leukocytes and platelets

End point title	Absolute values of the hematology parameters: leukocytes and platelets[27]

End point description:

Blood samples were collected for the analysis of hematology parameters including leukocytes and platelets. 99999 indicates that standard deviation could not be calculated as a single participant was analyzed. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment. Only those participants (pregnant women) with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

At Baseline (Day 1), Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 and Week 32 of study

Notes:

[27] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[28]			
Units: Giga cells per Liter				
arithmetic mean (standard deviation)				
Leukocytes, Baseline (Day 1), n=4	6.48 (± 1.415)			
Leukocytes, Week 4, n=4	7.88 (± 2.095)			
Leukocytes, Week 8, n=4	8.43 (± 1.959)			
Leukocytes, Week 12, n=4	9.15 (± 2.053)			
Leukocytes, Week 16, n=4	9.23 (± 1.821)			
Leukocytes, Week 20, n=4	10.03 (± 2.848)			
Leukocytes, Week 24, n=1	12.60 (± 99999)			
Leukocytes, Week 32, n=2	5.85 (± 0.636)			
Platelets, Baseline (Day 1), n=4	204.8 (± 37.03)			
Platelets, Week 4, n=4	200.5 (± 2.38)			
Platelets, Week 8, n=4	220.8 (± 16.07)			
Platelets, Week 12, n=4	195.5 (± 25.38)			
Platelets, Week 16, n=4	198.0 (± 10.80)			
Platelets, Week 20, n=4	216.5 (± 10.91)			
Platelets, Week 24, n=1	250.0 (± 99999)			

Platelets, Week 32, n=2	206.0 (± 24.04)			

Notes:

[28] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in hematology parameters: leukocytes and platelets

End point title	Change from Baseline in hematology parameters: leukocytes and platelets[29]

End point description:

Blood samples were collected for the analysis of hematology parameters including leukocytes and platelets. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. 99999 indicates that standard deviation could not be calculated as a single participant was analyzed. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment. Only those participants (pregnant women) with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Primary

End point timeframe:

Baseline and at Week 4, Week 8, Week 12, Week 16, Week 20, Week 24 and Week 32 of study

Notes:

[29] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[30]			
Units: Giga cells per Liter				
arithmetic mean (standard deviation)				
Leukocytes, Week 4, n=4	1.40 (± 1.817)			
Leukocytes, Week 8, n=4	1.95 (± 2.047)			
Leukocytes, Week 12, n=4	2.68 (± 1.173)			
Leukocytes, Week 16, n=4	2.75 (± 1.654)			
Leukocytes, Week 20, n=4	3.55 (± 2.340)			
Leukocytes, Week 24, n=1	4.90 (± 99999)			
Leukocytes, Week 32, n=2	-0.65 (± 1.061)			
Platelets, Week 4, n=4	-4.3 (± 39.09)			
Platelets, Week 8, n=4	16.0 (± 33.44)			
Platelets, Week 12, n=4	-9.3 (± 39.08)			
Platelets, Week 16, n=4	-6.8 (± 47.16)			
Platelets, Week 20, n=4	11.8 (± 45.49)			
Platelets, Week 24, n=1	10.0 (± 99999)			
Platelets, Week 32, n=2	-4.0 (± 50.91)			

Notes:

[30] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants (pregnant women) who discontinued the treatment due to adverse events (AE)

End point title	Number of participants (pregnant women) who discontinued the treatment due to adverse events (AE)[31]

End point description:

An AE is any untoward medical occurrence in a participants or clinical investigation participant, temporally associated with the use of a study treatment. Number of participants (pregnant women) who discontinued the treatment due to adverse events have been presented. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment.

End point type	Primary

End point timeframe:

Up to Week 292

Notes:

[31] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[32]			
Units: Participants	0			

Notes:

[32] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants (pregnant women) demonstrated congenital malformations

End point title	Number of participants (pregnant women) demonstrated congenital malformations[33]

End point description:

Data for participants (pregnant women) demonstrated congenital malformations was reported. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment.

End point type	Primary

End point timeframe:

At delivery (up to Week 40 of pregnancy)

Notes:

[33] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[34]			
Units: Participants	0			

Notes:

[34] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants (pregnant women) with adverse events (AE) as per severity grades

End point title	Number of participants (pregnant women) with adverse events (AE) as per severity grades[35]

End point description:

Number of participants (pregnant women) with adverse events (AE) as per severity grades were presented. Grade 1 is mild, grade 2 is moderate, grade 3 is severe or medically significant but not immediately life-threatening and grade 4 is life-threatening consequences; urgent intervention required. Safety Population comprised of all participants (pregnant women) who received at least one dose of study treatment.

End point type	Primary

End point timeframe:

Up to 292 Weeks

Notes:

[35] - 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: There are no statistical data to report

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[36]			
Units: Participants				
number (not applicable)				
Grade 1	2			
Grade 2	2			
Grade 3	0			
Grade 4	0			

Notes:

[36] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Cmax (tmax) for dolutegravir

End point title	Time to Cmax (tmax) for dolutegravir

End point description:

Blood samples were collected at indicated timepoints for PK analysis of dolutegravir at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum.

End point type	Secondary

End point timeframe:

Pre-dose and at 1, 2, 3, 4, 6, 8, 12, 24 hours post-dose at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[37]			
Units: Hours				
arithmetic mean (standard deviation)				
Trimester 2 (Weeks 18-26 of pregnancy)	3.508 (± 1.7082)			
Trimester 3 (Weeks 30-36 of pregnancy)	2.729 (± 0.4877)			
8-12 Weeks Postpartum	4.242 (± 2.0522)			

Notes:

[37] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Predose concentration (C0) for dolutegravir

End point title	Predose concentration (C0) for dolutegravir

End point description:

Blood samples were collected at indicated timepoints for PK analysis of dolutegravir at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum.

End point type	Secondary

End point timeframe:

Pre-dose at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[38]			
Units: Nanograms per milliliter				
geometric mean (confidence interval 95%)				
Trimester 2 (Weeks 18-26 of pregnancy)	666.9 (149.5 to 2974.6)			
Trimester 3 (Weeks 30-36 of pregnancy)	1084.6 (676.7 to 1738.3)			
8-12 Weeks Postpartum	1225.0 (522.8 to 2870.1)			

Notes:

[38] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Unbound DTG concentrations in plasma at 3 and 24 hours post dose of dolutegravir

End point title	Unbound DTG concentrations in plasma at 3 and 24 hours post dose of dolutegravir

End point description:

Blood samples were collected at indicated timepoints for PK analysis of dolutegravir at Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum.

End point type	Secondary

End point timeframe:

At 3 hours and 24 hours post dose in Trimester 2 (Weeks 18-26 of pregnancy), Trimester 3 (Weeks 30-36 of pregnancy) and at 8-12 Weeks postpartum

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[39]			
Units: Micrograms per milliliter				
geometric mean (confidence interval 95%)				
At 3 hours post dose in Trimester 2	7.856 (4.370 to 14.122)			
At 3 hours post dose in Trimester 3	7.371 (4.594 to 11.827)			
At 3 hours post dose 8-12 Weeks postpartum	6.898 (4.360 to 10.914)			
At 24 hours post dose in Trimester 2	1.798 (0.887 to 3.644)			
At 24 hours post dose in Trimester 3	2.065 (1.229 to 3.471)			
At 24 hours post dose 8-12 Weeks postpartum	2.881 (1.503 to 5.520)			

Notes:

[39] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Total DTG concentrations in plasma from cord blood and maternal blood at the time of delivery

End point title	Total DTG concentrations in plasma from cord blood and maternal blood at the time of delivery

End point description:

Blood samples were collected at the time of delivery for PK analysis of dolutegravir.

End point type	Secondary

End point timeframe:

At delivery (up to Week 40 of pregnancy)

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[40]			
Units: Nanograms per milliliter				
arithmetic mean (standard deviation)				
Cord plasma concentration	1436.0 (± 1287.43)			
Maternal plasma concentration	1806.3 (± 1125.04)			

Notes:

[40] - Pharmacokinetic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants (pregnant women) with treatment-emergent genotypic and/or phenotypic resistance who met confirmed virologic withdrawal criteria

End point title	Number of participants (pregnant women) with treatment-emergent genotypic and/or phenotypic resistance who met confirmed virologic withdrawal criteria

End point description:

Number of participants (pregnant women) with treatment-emergent genotypic and/or phenotypic resistance who met confirmed virologic withdrawal criteria are presented. Genotypic and phenotypic analyses were carried out by Monogram Biosciences using, but not limited to, their Standard Phenosense and GenoSure testing methods for protease (PRO) and reverse transcriptase (RT), or with their GeneSeq Integrase and PhenoSense Integrase assays. Intent-to-Treat Exposed (ITT-E) Population includes all participants (pregnant women) who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 32 of study

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[41]			
Units: Participants				
Participants with genotypic resistance	0			
Participants with phenotypic resistance	0			

Notes:

[41] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants (pregnant women) with live birth outcome categories

End point title	Number of participants (pregnant women) with live birth outcome categories

End point description:

Participants (pregnant women) with following live birth outcome categories are reported- Vaginal Birth, Planned Caesarean Section, Unscheduled Caesarean Section and Preterm Delivery. Safety Population comprised of all participants (Pregnant Women) who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

At delivery (up to Week 40 of pregnancy)

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[42]			
Units: Participants				
Vaginal Birth	1			
Planned Caesarean Section	2			
Unscheduled Caesarean Section	1			
Preterm Delivery	1			

Notes:

[42] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Gestational Age of infants

End point title	Gestational Age of infants

End point description:

Gestational age is defined as the number of weeks between the first day of the mother's last normal menstrual period and the day of birth. Data for gestational age of infants has been presented. Analysis was performed on Infant Population which consisted of infants born to pregnant women who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

At birth

End point values	DTG/ABC/3TC - Infant			
Subject group type	Subject analysis set			
Number of subjects analysed	4[43]			
Units: Weeks				
arithmetic mean (standard deviation)	38.3 (± 1.71)			

Notes:
[43] - Infant Population

Statistical analyses

No statistical analyses for this end point

Secondary: Neonatal length and head circumference at birth

End point title	Neonatal length and head circumference at birth

End point description:

Data for neonatal length and head circumference at birth are reported. Analysis was performed on Infant Population which consisted of infants born to pregnant women who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

At birth

End point values	DTG/ABC/3TC - Infant			
Subject group type	Subject analysis set			
Number of subjects analysed	4[44]			
Units: Centimeter				
arithmetic mean (standard deviation)				
Neonatal Length	51.5 (± 3.11)			
Neonatal Head Circumference	34.9 (± 1.65)			

Notes:
[44] - Infant Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of infants by their weight categories at birth

End point title	Number of infants by their weight categories at birth

End point description:

Weight of infants at birth were categorized as: Small for Gestational Age (SGA) defined neonates under the 10th percentile in weight, Appropriate for Gestational Age (AGA) characterized neonates between the 10th and 90th percentiles in weight and Large for Gestational Age (LGA) referred to neonates over the 90th percentile in weight. Analysis was performed on Infant Population which consisted of infants born to pregnant women who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

At birth

End point values	DTG/ABC/3TC - Infant			
Subject group type	Subject analysis set			
Number of subjects analysed	4[45]			
Units: Participants				
LGA	0			
AGA	4			
SGA	0			

Notes:

[45] - Infant Population

Statistical analyses

No statistical analyses for this end point

Secondary: Neonatal Weight at birth

End point title	Neonatal Weight at birth

End point description:

Data for neonatal weight at birth has been reported. Analysis was performed on Infant Population which consisted of infants born to pregnant women who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

At birth

End point values	DTG/ABC/3TC - Infant			
Subject group type	Subject analysis set			
Number of subjects analysed	4[46]			
Units: Grams				
arithmetic mean (standard deviation)	3262.5 (± 731.36)			

Notes:

[46] - Infant Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of infants by Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score at 1 and 5 minutes after birth

End point title	Number of infants by Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score at 1 and 5 minutes after birth

End point description:

APGAR is a quick test to assess the health of new born. The test is performed at 1 and 5 minutes after birth. APGAR scale is determined by evaluating the new born on five categories (appearance, pulse, grimace, activity and respiration) on a scale from zero to two with 2 being the best score, then summing up the values obtained from all five categories. APGAR score ranges from 0 to 10 (Higher score indicates better health) where a score of 7 and above is normal. Number of infants by APGAR score at 1 and 5 minutes after birth are presented. Analysis was performed on Infant Population which consisted of infants born to pregnant women who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

1 and 5 minutes after birth

End point values	DTG/ABC/3TC - Infant			
Subject group type	Subject analysis set			
Number of subjects analysed	4[47]			
Units: Participants				
1 Minute, Score 0 to 6	0			
1 Minute, Score 7 to 10	4			
5 Minute, Score 0 to 6	0			
5 Minute, Score 7 to 10	4			

Notes:

[47] - Infant Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants (pregnant women) with plasma Human Immunodeficiency Virus type 1 (HIV-1) Ribonucleic Acid (RNA) <50 copies/milliliter (c/mL) by visit

End point title	Percentage of participants (pregnant women) with plasma Human Immunodeficiency Virus type 1 (HIV-1) Ribonucleic Acid (RNA) <50 copies/milliliter (c/mL) by visit

End point description:

Percentage of participants (pregnant women) with plasma HIV-1 RNA <50 c/mL are presented. Plasma samples were collected for quantitative analysis of HIV-1 RNA. Only those participants (pregnant women) with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

At Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28 and Week 32 of study

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[48]			
Units: Percentage of participants				
Week 4, n=4	100			
Week 8, n=4	100			
Week 12, n=4	100			
Week 16, n=4	100			
Week 20, n=4	100			
Week 24, n=2	100			
Week 28, n=1	100			
Week 32, n=2	100			

Notes:

[48] - Intent-to-Treat Exposed Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants (pregnant women) with plasma HIV-1 RNA <400 c/mL by visit

End point title	Percentage of participants (pregnant women) with plasma HIV-1 RNA <400 c/mL by visit

End point description:

Percentage of participants (pregnant women) with plasma HIV-1 RNA <400 c/mL are presented. Plasma samples were collected for quantitative analysis of HIV-1 RNA. Only those participants (pregnant women) with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

At Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28 and Week 32 of study

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[49]			
Units: Percentage of participants				
Week 4, n=4	100			
Week 8, n=4	100			
Week 12, n=4	100			
Week 16, n=4	100			
Week 20, n=4	100			
Week 24, n=2	100			
Week 28, n=1	100			
Week 32, n=2	100			

Notes:

[49] - Intent-to-Treat Exposed Population

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of cluster of differentiation 4 (CD4+) T cell counts by visit

End point title	Absolute values of cluster of differentiation 4 (CD4+) T cell counts by visit

End point description:

Blood samples were collected for the analysis of CD4+ T cell counts using cytometry. 99999 indicates that standard deviation could not be calculated as a single participant was analyzed. Only those

participants (pregnant women) with data available at the specified data points were analyzed represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

At Baseline (Day 1), Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28 and Week 32 of study

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[50]			
Units: Cells per cubic millimeter				
arithmetic mean (standard deviation)				
Baseline (Day 1), n=4	476.3 (± 123.31)			
Week 4, n=4	569.5 (± 238.51)			
Week 8, n=4	569.8 (± 296.43)			
Week 12, n=4	575.0 (± 331.22)			
Week 16, n=4	626.8 (± 270.63)			
Week 20, n=4	791.5 (± 524.96)			
Week 24, n=2	874.5 (± 516.90)			
Week 28, n=1	488.0 (± 99999)			
Week 32, n=2	677.5 (± 40.31)			

Notes:

[50] - Intent-to-Treat Exposed Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+ T cell counts by visit

End point title	Change from Baseline in CD4+ T cell counts by visit

End point description:

Blood samples were collected for the analysis of CD4+ T cell counts using cytometry. Baseline value (Day 1) is the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. 99999 indicates that standard deviation could not be calculated as a single participant was analyzed. Only those participants (pregnant women) with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and at Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28 and Week 32 of study

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[51]			
Units: Cells per cubic millimeter				
arithmetic mean (standard deviation)				
Week 4, n=4	93.3 (± 124.64)			
Week 8, n=4	93.5 (± 174.54)			
Week 12, n=4	98.8 (± 208.50)			
Week 16, n=4	150.5 (± 148.73)			
Week 20, n=4	315.3 (± 402.00)			
Week 24, n=2	353.0 (± 332.34)			
Week 28, n=1	98.0 (± 99999)			
Week 32, n=2	246.0 (± 97.58)			

Notes:

[51] - Intent-to-Treat Exposed Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants (pregnant women) with disease progression

End point title	Number of participants (pregnant women) with disease progression

End point description:

Disease progression included HIV-associated conditions, acquired immunodeficiency syndrome (AIDS) and death. Number of participants (pregnant women) with disease progression to Centers for Disease Control and Prevention (CDC) class C or death have been presented.

End point type	Secondary

End point timeframe:

Up to Week 32 of study

End point values	DTG/ABC/3TC - Mother			
Subject group type	Reporting group			
Number of subjects analysed	4[52]			
Units: Participants	0			

Notes:

[52] - Intent-to-Treat Exposed Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality, serious and non-serious adverse events were collected up to maximum of 292weeks (data cut-off date:15-Mar-2021). Safety population comprised of all pregnant women who received at least one dose of study treatment

Adverse event reporting additional description:

All-Cause Mortality and Adverse events was collected only in pregnant women (study participants) and not in infants, as they are not considered as enrolled per study design. Results are based on Primary analysis up to maximum of 292weeks (data cut-off date:15-Mar-2021), and additional results will be provided within one year after study completion.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	DTG/ABC/3TC - Mother

Reporting group description:

Participants (pregnant women) received fixed dose combination (FDC) tablet of dolutegravir (DTG) 50 milligrams (mg), abacavir (ABC) 600 mg and lamivudine (3TC) 300 mg once daily, with or without food.

Serious adverse events	DTG/ABC/3TC - Mother		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Pregnancy, puerperium and perinatal conditions			
Premature baby			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	DTG/ABC/3TC - Mother		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Migraine subjects affected / exposed occurrences (all)	 2 / 4 (50.00%) 2 1 / 4 (25.00%) 2		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	 2 / 4 (50.00%) 2		
Gastrointestinal disorders Dyspepsia subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Dermatitis allergic subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1		
Renal and urinary disorders Nephropathy subjects affected / exposed occurrences (all)	 2 / 4 (50.00%) 4		
Musculoskeletal and connective tissue disorders Intervertebral disc protrusion subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Infections and infestations Cystitis subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		

Gastroenteritis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	5		
Oral herpes			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Vaginal infection			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Respiratory tract infection viral			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 April 2014	Amendment 01: Editorial changes, including corrections of minor typographical errors and/or inconsistencies in the Time and Events Table 6 and the protocol, inclusion of infant Human Immunodeficiency Virus (HIV) status if available, and edits to Appendix 3 wording
23 April 2014	Amendment 02: Specifically, in the Summary of Revisions, page 1, the reader is referred to Time and Events Table 6; it should be Table 4. The Division of Acquired Immunodeficiency Syndrome (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events was added as a new appendix, changing numbers of other appendices. It's inclusion also needed to be added to Appendix 6. Lastly, where the Summary of Revisions says Appendix 3, it should be Appendix 4.
19 June 2018	Amendment 03: Changes were made to the protocol to manage and mitigate risks following identification of a potential safety issue related to neural tube defect in infants born to women with exposure to dolutegravir at the time of conception. The Rationale and Risk Assessment sections (Section 1.2. and Section 1.3.1.) were updated to include language regarding risk and mitigation of neural tube defects. The Withdrawal Criteria (Section 4.5.) were updated to include a reminder that post-delivery, participants who desire to be pregnant, or who state they are not willing/no longer willing to comply with the approved pregnancy avoidance methods, should be withdrawn from the study. The Time and Events table (Section 6.) was updated to include a footnote to clarify the requirement for pregnancy tests post-delivery, and a reminder for investigators to check at every post-delivery visit that participants are avoiding pregnancy. Contraception Requirements for the Post-Partum and Continuation Phases (Section 6.5.4.8.) were updated with the most recent list of 'highly effective methods for avoiding pregnancy in females of reproductive potential', which excludes the double barrier method of contraception. Administrative updates were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported