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- *Aggregate data will be included; with any direct reference to individual patients excluded*

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TITLE PAGE

Information Type: ViiV Healthcare Epidemiology Final Study Report

Title: A multi-site observational study to assess safety and effectiveness of prenatal exposure to Dolutegravir in pregnant individuals living with HIV

Phase: IV

Compound Number: GSK1349572 (Tivicay), GSK2619619 (GSK1349572+GR109714+GI265235, Triumeq), GSK3365791 (GSK1349572+GSK1329758, Juluca), GSK 3515864 (GSK1349572+GR109714, Dovato)

Effective Date: 18-OCT-2023

Subject: Safety and effectiveness of Dolutegravir in pregnancy

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SPONSOR SIGNATORY SIGNATURE PAGE

I have read this report and confirm that to the best of my knowledge this report accurately describes the conduct and results of study 212976.

PPD

Primary Author/ Project officer	25-SEP-2023 **Date**

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Jens-Ulrich Stegmann ViiV QPPV	18-Oct-2023 **Date**

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1 LIST OF ABBREVIATIONS

Abbreviation	Description
3TC	Lamivudine
ABC	Abacavir
ACOG	American College of Obstetrics and Gynecology
ADRs	Adverse Drug Reactions
AE	Adverse Event
AIDS	Acquired Immune Deficiency Syndrome
APGAR	Appearance, Pulse, Grimace, Activity, Respiration
APR	Antiretroviral Pregnancy Registry
ART	Antiretroviral Therapy
ARV	Antiretroviral
BMI	Body mass index
CD4	Cluster of Differentiation 4
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CMV	Cytomegalovirus
DOC	Date of Conception
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDD	Estimated date of delivery
EFV	Efavirenz
EPPICC	The European Pregnancy and Paediatric HIV Cohort Collaboration
FDC	Fixed Dose Combination
HCPs	Healthcare Providers
HIV	Human Immunodeficiency Virus
HR	Hazard ratio
HSR	Hypersensitivity Reaction
IMPAACT	International Maternal Paediatric Adolescent AIDS Clinical Trial Network
INSTI	Integrase Strand Transfer Inhibitor
IRBs	Institutional Review Boards
LBW	Low birth weight
LCT	Liver Chemistry Test
LMP	Last Menstrual Period
MACDP	Metropolitan Atlanta Congenital Defects Program
MCV	Mean corpuscular volume
NNRTI	Non-nucleoside analog reverse transcriptase inhibitors
NRTI	Nucleoside analog reverse transcriptase inhibitors
NTDs	Neural tube defects
OR	Odds ratio
PI	Protease inhibitors
PT	Preferred term
RPV	Rilpivirine
SADRs	Serious Adverse Drug Reactions

SAE	Serious Adverse Event
SOC	System organ class
TBDR	Texas Birth Defects Registry
TORCH	Toxoplasmosis, Other, Rubella, Cytomegalovirus, and Herpes
UK	United Kingdom
US	United States
VL	Viral Load
WHO	World Health Organization

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3 ABSTRACT

Title

A multi- site observational study to assess safety and effectiveness of prenatal exposure to Dolutegravir in pregnantindividuals with HIV.

Subject

Safety and effectiveness of Dolutegravir in pregnancy

Background

Dolutegravir (DTG) (TIVICAY) is a 2-metal binding integrase inhibitor (integrase strand transfer inhibitor: INSTI) licensed for the treatment of Human Immunodeficiency Virus-1 (HIV) infection in adults and children over 12 years of age as part of combination antiretroviral (ARV) therapy. It was first approved on 12 August 2013 in the United States (US) and is also licensed for use in children over 6 years of age in the US.

Dolutegravir/abacavir sulphate (ABC)/lamivudine (3TC) (TRIUMEQ) is a single tablet containing DTG and the two nucleoside analog reverse transcriptase inhibitors (NRTIs) ABC (600 mg) and 3TC (300 mg), indicated for the treatment of HIV infection in adults and adolescents above 12 years of age weighing at least 40 kg. DTG/ABC/3TC fixed dose combination (FDC) tablet was first approved on 22 August 2014 in the US.

Dolutegravir/rilpivirine (DTG/RPV) (JULUCA) is a FDC tablet containing DTG (50 mg) in combination with the non-nucleoside analog reverse transcriptase inhibitor (NNRTI) rilpivirine (RPV 25 mg). It is licensed for the treatment of HIV-1 infection in adults who are virologically suppressed without known or suspected resistance to either component. DTG/RPV FDC was first approved in the US on 21 November 2017.

Dolutegravir/lamivudine (DTG/3TC) (DOVATO) is a FDC tablet containing DTG (50 mg) in combination with 3TC (300 mg). It is licensed for HIV-1 infection in adults as a complete treatment regimen for the treatment of HIV-1 infection where there is no known or suspected resistance to the INSTI class, or to 3TC. DTG/3TC FDC was first approved in the US on 08 April 2019.

This is a non-interventional study to assess the safety and effectiveness of DTG use in pregnancy in “real world” setting in the United States. The study collected data through retrospective review and abstraction of patient medical records from participating clinical sites. There were no study related interventions or study procedures related to patient care and all treatment decisions were made by the healthcare providers prior to data abstraction.

Research questions and objectives

The aim for this study was to assess the safety and effectiveness of DTG use pregnant individuals living with HIV, in a “real world” setting.

Study Aims:

1. To describe the demographic and clinical characteristics of pregnant individuals exposed to DTG

2. To assess the frequency of birth defects among neonates, with prenatal exposure to DTG, categorized by timing of earliest exposure (peri-conception, later first trimester, second trimester and third trimester)

3. To describe non-defect pregnancy and neonatal outcomes of the DTG exposed pregnancies

4. To assess virologic outcomes among pregnant individuals on DTG based treatment regimen

Study design

This was a retrospective cohort study of data collected by review and abstraction of patient medical records at participating clinical sites.

Study Population and setting

The study population included all pregnant individuals living with HIV, aged ≥18 years who were exposed to DTG during periconception and/or pregnancy.

There was no comparator arm used in this study Data from external sources like the Centers for Disease Control and Prevention's (CDC) birth defects surveillance system the Metropolitan Atlanta Congenital Defects Program (MACDP), the Texas Birth Defects Registry (TBDR) and the Antiretroviral Pregnancy Registry (APR) data were used as external comparators to put the findings from this study in context.

Syneos Health operationalized the study on behalf of the sponsor (ViiV Healthcare). The study protocol was approved by a central Institutional Review Board (IRB).

4 AMENDMENTS AND UPDATES

None

5 BACKGROUND

Dolutegravir (DTG) (TIVICAY) is a 2-metal binding integrase inhibitor (integrase strand transfer inhibitor: INSTI) licensed for the treatment of Human Immunodeficiency Virus-1 (HIV) infection in adults and children over 12 years of age as part of combination antiretroviral (ARV) therapy. It was first approved on 12 August 2013 in the United States (US) and is also licensed for use in children over 6 years of age in the US.

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In animal and ex vivo human placenta perfusion studies, DTG has been shown to have a high penetration across the placenta, unlike some other ARV, where this might protect a developing embryo against vertical HIV transmission but might also increase the risk of adverse birth outcomes [FDA, Tivicay, 2017; Lewis, 2016]. In animal toxicology studies [Rimawi, 2017], there has been no evidence for adverse effects from DTG treatment during pregnancy [Bornhede, 2018].

In the most recent (March 2022) report from a birth outcome surveillance study in Botswana (Tsepamo Study), there were 10 cases of neural tube defects (NTD) reported out of 9,460 deliveries (0.11%) [Zash, 2022] to individuals who were exposed to dolutegravir-containing regimens at the time of conception, which is no longer statistically different than exposure in any of the comparison groups, including exposure to non-dolutegravir-containing regimens at the time of conception and HIV-uninfected individuals. This constitutes a further decline in NTD prevalence in deliveries of individuals exposed to dolutegravir-containing regimens at the time of conception reported in March 2021 (0.15%). In addition, an ongoing birth surveillance study in Eswatini [Gill 2023], with methodology similar to the Botswana Tsepamo study, reported

on birth surface defect surveillance conducted September 2021 through September 2022 at five hospitals in four regions of Eswatini that account for 73% of all births in the country in 2021. The study included 7,554 pregnant individuals living with HIV, 4,832 of whom were receiving dolutegravir regimens at conception, and 17,270 individuals without HIV infection. NTD prevalence was 0.08% (n=4) in individuals with HIV receiving dolutegravir at conception and 0.08% (n=13) in individuals without HIV infection; the prevalence was 0.16% (n=2) in the smaller number of 1,248 individuals receiving nondolutegravir regimens at conception. Combined with the Tsepamo data, there are now >14,000 births among individuals on dolutegravir at conception with 14 NTDs identified, giving a weighted NTD prevalence of 0.098%, which is not significantly different than non-dolutegravir regimens at conception or individuals without HIV infection in either country. These data do not support an association of NTD and preconception dolutegravir.

Data from The European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC) [Vannappagari 2019], the Canadian Perinatal HIV Surveillance Program [Money, 2019], the French National Health database (SNDS) analysis [Chouchana, 2019], and the National Cohort Study of Dolutegravir and Pregnancy Outcomes in Brazil [Pereira 2019] did not show an increased risk for NTDs or other birth defects.

The Antiretroviral Pregnancy Registry (APR), the second largest source of data on use of DTG in pregnancy, had data on 1464 prospectively reported pregnancies with exposure to DTG as of 31st January 2023. Of them, 775 pregnancies reported exposure at conception, 184 pregnancies with exposure later during the first trimester, 356 pregnancies during the second trimester, 148 pregnancies during the third trimester and 1 was during an unknown trimester. The 1464 pregnancies with exposure to DTG resulted in 1498 outcomes including 1378 (92.0%) live births, 18 (1.2%) still births, 43 (2.9%) induced abortions, and 59 (3.9%) spontaneous abortions. Among the live births, 54 (3.9%) reported birth defects. For periconception exposures, the defect prevalence is 3.01% (21/698), 95% CI:1.87-4.56. There was one neural tube defect (anencephaly) with exposure to DTG at the time of conception. Among the 1265 singleton, live births without birth defects, 140 (11.1%) were preterm (<37 weeks of gestation); 156 (12.3%) reported low birth weight (<2500 grams) and 28 (2.2%) reported very low birth weight (<1500 grams). While limited in sample size to reach definitive conclusions, the latest data from the APR do not demonstrate an increased risk of overall birth defects with DTG use above the population expected rate of defects (2.72 - 4.17/ 100 live births) reported in the Centers for Disease Control and Prevention's (CDC) birth defects surveillance system, the Metropolitan Atlanta Congenital Defects Program (MACDP) and the Texas Birth Defects Registry (TBDR). To detect rare defects such as neural tube defects, approximately 2000 pregnancies with drug exposure are needed to determine a three-fold increased risk of the event occurring [Watts, 2007]. Although one neural tube defect has been identified in 281 pregnancy exposures to DTG at conception (1/289 pregnancy outcomes and 1/248 live births), the numbers remain too small for final conclusions.

A number of smaller post-marketing cohorts and clinical studies with DTG-exposed pregnancy have been published. Cohort sizes range from less than five to 50 and most are from Europe: France [Sibiude, 2019], Sweden [Bornhede, 2018], the US [Grayhack,

2018], Germany [Weissmann, 2018], Belgium [Henrard, 2017], London, UK [Haidari, 2018; Simons, 2017]; Central and Eastern Europe [Kowalska, 2018] and Italy [Mondi, 2019], There are also, the ADVANCE and NAMSAL ANRS 12313 clinical studies being conducted in Africa [Venter, 2019; Chandiwana, 2019; NAMSAL ANRS 12313 Study Group, 2019]. No neural tube defects were identified in these cohorts and no other important concerns relating to use of DTG in pregnancy were identified. In addition, a number of studies have provided information relating to use of DTG later in pregnancy, including the IMPAACT (International Maternal Paediatric Adolescent AIDS Clinical Trial network) P1026s study [Mulligan, 2018], the DolPHIN-1 and DolPHIN-2 studies [Waitt, 2018; Kintu, 2019] and the PANNA study (Pharmacokinetics of newly developed ANtiretroviral agents in HIV-infected pregNAnt women) [Bollen, 2018; Colbers, 2019]. No safety concerns relating to use of DTG in later pregnancy have been identified from these studies.

This is a non-interventional study to assess the safety and effectiveness of DTG use in pregnancy in "real world" setting in the United States. The study collected data through retrospective review and abstraction of patient medical records from participating clinical sites. There were no study related interventions or study procedures related to patient care and all treatment decisions were made by the healthcare providers prior to data abstraction.

6 RESEARCH QUESTION AND OBJECTIVES

The aim for this study was to assess the safety and effectiveness of DTG use in pregnant individuals living with HIV in a "real world" setting.

Study Aims:

1. To describe the demographic and clinical characteristics of pregnant individuals exposed to DTG

2. To assess the frequency of birth defects among neonates, with prenatal exposure to DTG, categorized by timing of earliest exposure (peri-conception, later first trimester, second trimester and third trimester)

3. To describe non-defect pregnancy and neonatal outcomes of the DTG exposed pregnancies

4. To assess virologic outcomes among pregnant individuals on DTG based treatment regimen

7 RESEARCH METHODS

7.1 Study Design

This was a retrospective cohort study of data collected by review and abstraction of patient medical records at participating study sites.

7.2 Study Population and Setting

The study population included all pregnant inviduals living with HIV, aged ≥18 years who were exposed to DTG during periconception and/or pregnancy.

7.2.1 Exposure Definitions

Main exposure of interest was DTG use during periconception and pregnancy. Data on timing of earliest exposure and duration of exposure to DTG was captured in detail.

Timing of earliest exposure to DTG**:** This was stratified into periconception period, later first trimester, second trimester and third trimester estimated using the first day DTG was known to have been taken. A patient may have had multiple exposures, defined in cases where there was reinitiation of therapy after a period of stoppage during pregnancy. Where available, reasons for stoppage were collected.

- *Periconception* – DTG exposure from 2 weeks before conception through 28 days after conception (up to 6 weeks of estimated gestational age)
- *Later 1st trimester* – Initial exposure started later in the 1st trimester, >28 days after conception (6 weeks estimated gestational age) through 13 weeks of gestational age
- *2nd trimester* – Exposure started after the 1st trimester ended (≥14 weeks through 27 weeks of estimated gestational age)
- *3rd trimester* – Exposure started after the 2nd trimester ended (≥28 weeks of estimated gestational age to delivery)

Duration of exposure: the number of days that the woman was known to have been exposed to DTG during her pregnancy. This was further categorized by number of days per trimester.

7.2.2 Outcome Definitions

7.2.2.1 Primary Outcomes

a. The primary effectiveness parameters were maternal viral load (VL) at delivery (<50 copies/mL & ≥200 copies/mL) and neonatal HIV status.
b. The primary safety parameters were spontaneous abortion, induced abortion, still birth, live birth, preterm birth, low birth weight and prevalence of birth defects.

Table 7-1 Definitions of pregnancy outcomes (aligned with APR definitions)

Pregnancy Outcome/ Birth Outcome	Definition
Spontaneous abortion	Death of a fetus or expulsion of the products of conception prior to 20 weeks gestation. Terminology may include missed abortion, blighted ovum, incomplete abortion, and inevitable abortion
Induced abortion	Voluntary termination of pregnancy
Stillbirth	Death of a fetus occurring at ≥20 weeks of gestation, or if the gestational age is unavailable, a fetus weighing ≥500 grams
Preterm birth	Birth of live infant at <37 weeks gestation (American College of Obstetrics and Gynecology [ACOG] standard definition); if gestational age not available, birth weight <2500 grams (CDC's MACDP criteria)
Severely preterm birth	Birth of live infant at <32 weeks gestation
Low birth weight	Birth weight of <2500 grams
Very low birth weight	Birth weight of <1500 grams
Extremely low birth weight	Birth weight of <1000 grams
Birth defects	Classified according to the APR classification of birth defects (modified MACDP classification)

Birth Defect – Detailed evaluation of birth defects, organ system classification and temporality assessment were performed by the study clinical geneticist (board certified in Clinical Genetics and Clinical Molecular Genetics), who is also the APR's teratologist.

A birth defect in this study followed the APR categorization schema and was defined as a) any major structural malformation or chromosomal defect diagnosed or with signs/symptoms before six years of age, in addition (2) on a case-by-case basis, patient to independent review, any cluster of two or more conditional abnormalities, or (3) on a case-by-case basis, patient to independent review, any structural or chromosomal defect detected in the prenatal evaluation of a pregnancy or in the gross or pathologic examination of an abortus, fetus, or deceased infant. The Registry excludes birth defects attributed to prematurity itself (e.g., patent ductus arteriosus, patent foramen ovale, and inguinal hernias).

Temporality Assessment of the birth defects: The determination of the probable association or non-association of the timing of the maternal ARV exposure in pregnancy relative to the probable timing of organogenesis of a defect.

7.2.2.2 Secondary Outcomes

a) All DTG related adverse events (AEs)
b) All DTG related serious adverse events (SAEs)

c) Virologic failure (>200 copies/mL)
d) Frequency of discontinuation of DTG in pregnancy, and where available reasons for discontinuation and VL at discontinuation
e) Where available, VL (<50 copies/mL & ≥200 copies/mL) during each of the three trimesters to assess suppression and at delivery

7.2.3 Confounders and Effect Modifiers

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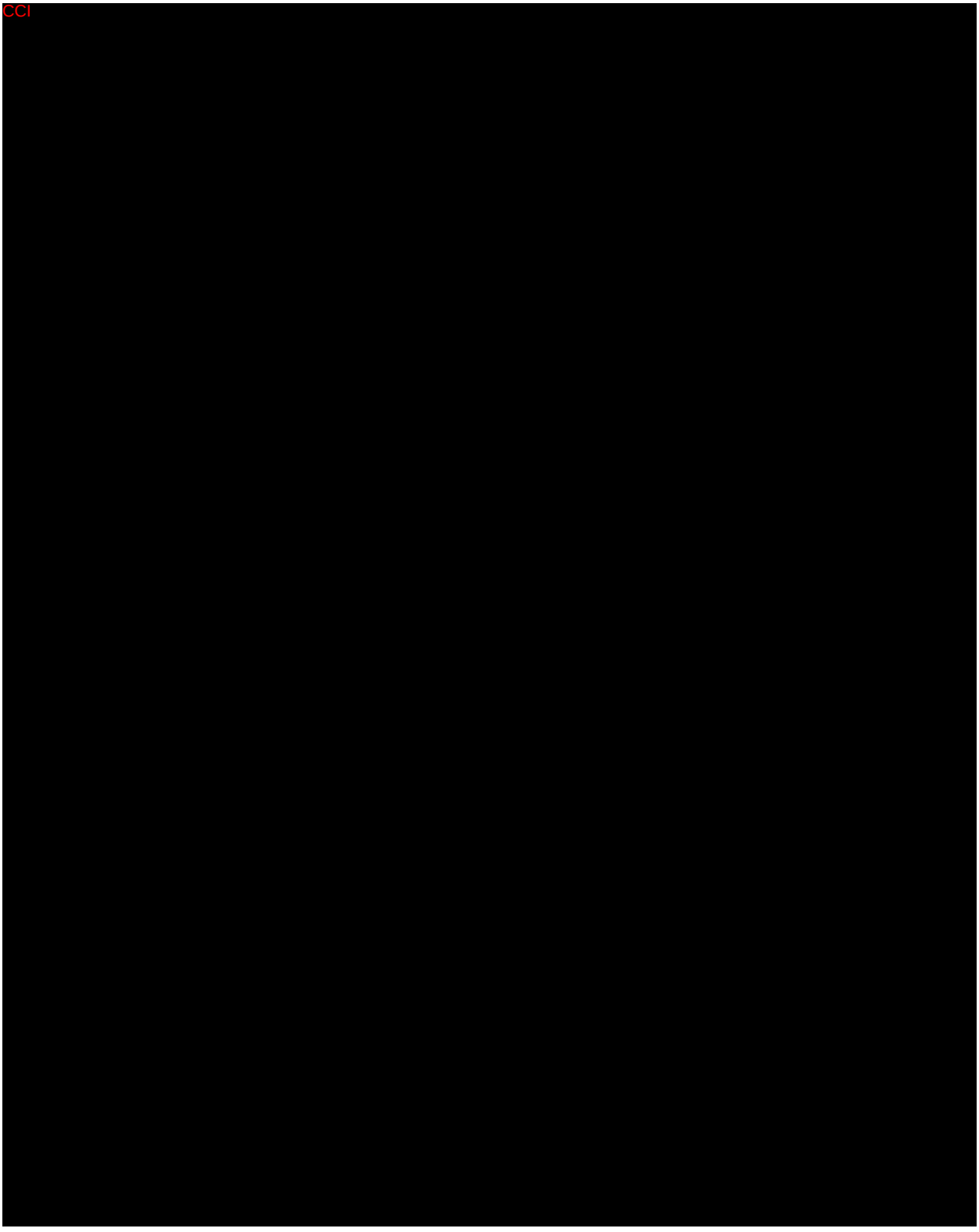

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7.3 Data Sources

Data was collected from all participating US sites. Following a central Institutional Review Board (IRB), clinical sites were contacted and asked to identify all individuals on DTG during pregnancy and extract medical chart data for these individuals. Data relevant to the study objectives wa abstracted by the participating site's team or by a Syneos Health team member from the individuals' medical records. The participants did not have to attend any additional visits or undergo any procedure above their routine standard of care. Anonymised data was collected either by electronic transfer of datasets from each site or entered into a secure electronic case report form (eCRF) platform dependent on their capabilities (there was no transferal of personal identifiers to Syneos Health).

Each eCRF was assigned a unique code for each individual for data reference purposes (the unique code enabled the depersonalization of data; where the participant's identifying information was replaced by an unrelated sequence of characters, only sites had access to the de-coded lists). Syneos Health did not have access to de-coded lists. Sites were monitored for data quality and accuracy as per the risk-based monitoring plan for the study.

The following data was collected if available for each participant CCI [redacted]

1. Baseline characteristics such as age, weight, height, BMI, ethnicity, medical history, history of previous pregnancies including complications (abruptio, eclampsia and preeclampsia) and outcomes, nadir CD4, prior or current Acquired Immune Deficiency Syndrome (AIDs) defining illness at time of starting pregnancy.
2. Date of start of pregnancy as Last Menstrual Period (LMP) or estimated Date of Conception (DOC) with appropriate identifier.
3. Date of starting DTG.
4. Date of stopping DTG or confirmation that DTG was continued to delivery.
5. Latest data on CD4 count, VL, ARV drug history with dates, within 6 months prior to the start of pregnancy, where available.
6. ARV drug history with dates of starting and reasons for stopping during pregnancy.
7. Co-morbidities and all co-medications including prenatal supplements.
8. Maternal history of seizures.
9. Maternal history of pregestational and gestational diabetes and fasting glucose & HbA1c levels at the time of pregnancy diagnosis and during each of the trimesters, when applicable.

10. Where available, HIV RNA and CD4 count data at time of enrolment and during pregnancy until delivery and also at time of starting DTG.
11. VL at DTG discontinuation during pregnancy, if applicable.
12. Resistance tests results of any HIV resistance tests performed during pregnancy.
13. All DTG related AEs and SAEs (Adverse Drug Reactions [ADRs] and Serious Adverse Drug Reactions [SADRs] as determined and documented in the medical record): timing in pregnancy, incidence and severity.
14. Pregnancy outcomes including spontaneous abortion, induced abortion, stillbirths, multiple births, live births, type of delivery (normal delivery, forceps delivery, or caesarean) and VL at delivery.
15. Birth outcomes including birth defects with date and other routinely collected data at birth such as gestational age, birth weight, Appearance, Pulse, Grimace, Activity, Respiration (APGAR) score.
16. Postpartum CD4 count and VL.
17. HIV status of the newborn infant.

There was no comparator arm used in this study. Data from MACDP, TBDR and the APR were used as external comparators to put the findings from this study in context.

7.4 Data Management

7.4.1 Data Transformation (Data Handling Conventions)

Data was handled in accordance with data handling guidelines provided to sites. The Study Monitor and Data Manager reviewed data on an on-going basis and raised any discrepancies with site staff, as required. Identified only by unique patient number, the deidentified data was transferred securely, and all transfers were fully documented.

7.5 Data Management

7.5.1 Essential Analyses

7.5.1.1 Primary Outcomes

The primary efficacy endpoints were maternal VL at delivery (<50 copies/mL & ≥200 copies/mL) and neonatal HIV status.

By visit summary tables for maternal HIV viral load values were provided by study strata and overall. Categories of <50 and ≥200 copies/mL of viral load at delivery were also presented.

An ordinal regression analysis was performed using maternal VL at delivery as dependent variable and study strata (trimester of DTG exposure) as independent variable. Odds ratios (95% confidence intervals) were provided in the statistical summary table.

Neonatal HIV status (positive vs. negative) was summarized for the infant by study strata and overall. Logistic models were applied to analyze the odds ratio between trimesters (using periconception period as reference).

7.5.1.2 Primary Safety Endpoints

The primary safety endpoints were pregnancy outcomes/birth outcomes, which included spontaneous abortion, induced abortion, stillbirths, live births, preterm births, low birth weight and prevalence of birth defects (definitions found in Table 7-1).

7.5.1.2.1 Analysis of Pregnancy and Infant Outcomes

The number and percentage of each pregnancy outcome (including live birth, stillbirth, spontaneous abortion, induced abortion, preterm birth, severely preterm birth, low birth weight, very low birth weight, extremely low birth weight) were reported by study strata and overall. Two-sided 95% confidence intervals were calculated using the exact binomial distribution (Clopper–Pearson method).

The following infant outcomes were summarized by study strata and overall:

- Gestational age at birth (in weeks)
- Gender
- Race
- Birth weight (grams)
- Birth length (cm)
- Head circumference (cm)
- APGAR scores at 5 min and 10 min
- Infant size which was calculated based on the 2006 World Health Organization (WHO) Child Growth Standards used to derive the z-scores for weight-for-age and sex. Infant size will be categorized as ≤10%, >10% and ≤50%, >50% and ≤90% and >90% based on the weight for gestational age at birth.

7.5.1.2.2 Prevalence of Birth Defects

Overall and stratum-specific point estimates and 2-sided 95% confidence intervals were calculated using the exact binomial distribution (Clopper-Pearson method) for prevalence of any birth defects, including subcategories such as polydactyly, ventricular septal defect, hypospadias and hemangioma. If the infant had more than one birth defect, it was counted once in each sub-category. Percentage of frequency of all birth defects were plotted.

Birth defects were also summarized by system organ class and preferred terms. By patient listing of birth defects was provided.

7.5.1.3 Secondary Analysis Endpoints

The secondary analysis endpoints included:

- All maternal DTG related AEs
- All DTG related SAEs

- Frequency of discontinuation of DTG in pregnancy, and where available reasons for discontinuation and VL at discontinuation.

7.5.1.4 Adverse Events

AEs were coded using MedDRA (version 22.0) system organ class (SOC) and preferred term (PT). The severity of AEs will be graded per the NCI CTCAE v4.0. Missing severity was imputed as "Severe" for summary purposes only.

AE summary tables present the following:

- Any maternal AEs
- Any maternal DTG related AEs
- Any infant AEs
- Any infant DTG related AEs

Maternal and infant adverse events were summarized, separately, by SOC and PT as follows:

- AEs
- AEs by maximum severity
- DTG related AEs
- DTG related AEs by maximum severity

AEs and SAEs were considered to be DTG related if the event value is reported as "Yes", "Unknown" or Missing for the "Event suspected to be related to DTG" question on the AE eCRF page.

For each patient, the event was counted only once within a SOC/PT combination. A patient may appear more than once if the patient has more than one event; however, the patient was counted only once in the overall category.

For the maximum severity tables, if a patient experienced more than 1 occurrence of the same AE, the occurrence with the greatest severity was used in the summary tables.

The number and percentage of individuals experiencing at least one occurrence of the event by study strata and overall was presented. The denominator in the calculation of all AE percentages was the number of individuals in the primary analysis population.

All AEs were listed by study strata, patient and then chronologically by date and time of onset. This listing includes all data collected in the eCRF.

7.5.2 Exploratory Analyses

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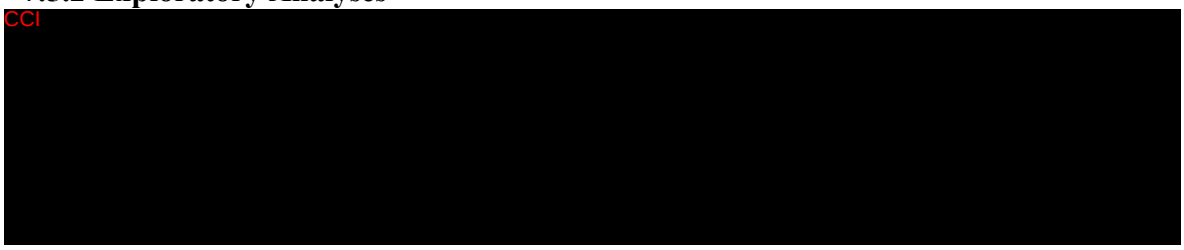

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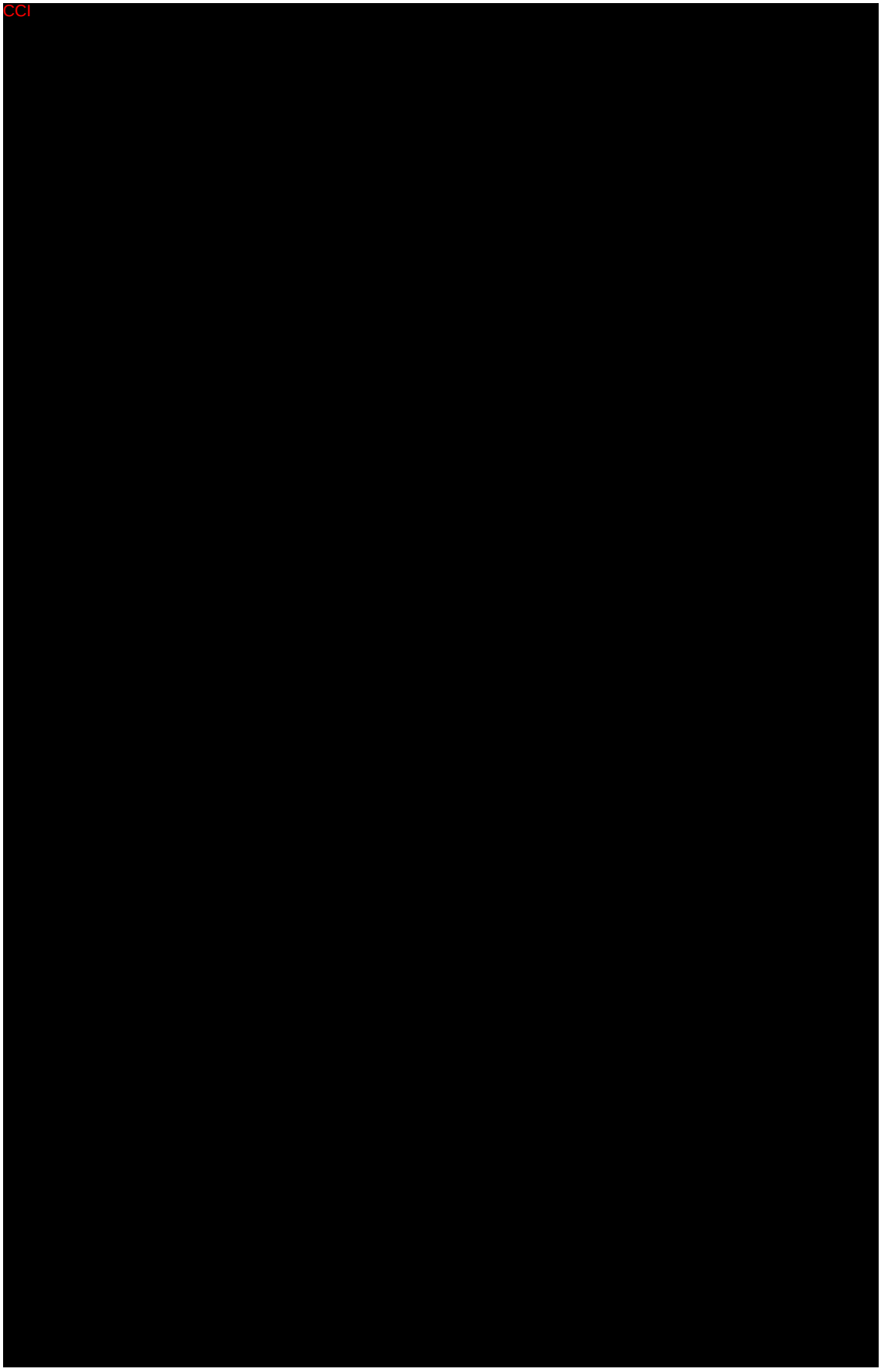

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7.5.3 General Considerations for Data Analyses

Analysis Populations:

- Primary Analysis Population: The primary analysis population included all consenting pregnant individuals living with HIV, aged ≥18 years who were enrolled into the study and had been exposed to DTG during periconception and/or pregnancy. This population was used for all summary tables (excluding Disposition).

There was no imputation of missing data. Missing data was treated as missing.

8 PROTECTION OF HUMAN INDIVIDUALS

8.1 Ethical Approval

Before the start of data collection, the protocol and other relevant material were submitted to ethics committees (EC), central Institutional Review Boards (IRBs) and local IRBs, as required. The sites did not begin any study activities until the site investigator had received written and dated approval from the IRB/ EC.

8.2 Patient Confidentiality

Sites routinely hold identifiable information on their individuals. All investigators and study site staff complied with the requirements of the current Data Protection Regulations in the United States with regard to the collection, storage, processing and disclosure of personal information and upheld the Regulations' core principles.

Personal information was to be collected, kept secure, and maintained in line with the following requirements:

- the creation of coded, depersonalised data where the participant's identifying information was replaced by an unrelated sequence of characters.
- secure maintenance of the data and the linking code in separate locations using encrypted digital files within password protected folders and storage media.
- limiting access to the minimum number of individuals necessary for quality control, audit, and analysis.

9 RESULTS

9.1 Participants

There were a total of 572 enrolled individuals; 484 individuals exposed to DTG that were included in the primary analysis and 88 invalid cases. Of the 484 exposed individuals in the primary analysis population, 195 were exposed periconception, 87 exposed later in the first trimester, 140 exposed in the second trimester, and 62 exposed in the third

trimester. (Table 9-1).

Table 9-1 Patient Disposition (All Enrolled Individuals)

	Periconception	Later First Trimester	Second Trimester	Third Trimester	Overall
All Enrolled Individuals[a]					572
Exposed to DTG	195	87	140	62	484
Primary Analysis Population[b]	195 (100)	87 (100)	140 (100)	62 (100)	484 (100)
Invalid case[c]					88

a All enrolled individuals include all individuals who signed the informed consent form.
b Primary Analysis Population includes all HIV positive pregnant individuals aged ≥18 years who are enrolled into the study and have been exposed to DTG during periconception and/or pregnancy.
c. Invalid cases are those that do not meet the criteria of the primary analysis population.
Note: Percentages are based on the numbers of individuals exposed to DTG in each column.

9.2 Descriptive Data including Baseline Characteristics

Individuals had a median age of 29.0 years (min, max=18,44), a median height of 162.500cm (min, max=142.20, 185.00), a median weight of 74.60kg (min, max=38.1, 169.1), and a median BMI of 28.125kg/m^2 (min, max=15.36, 63.96). The majority of individuals were black or African American (74.8%) and not Hispanic or Latino (79.3%). Demographics were consistent across all exposure timing categories (Table 9-2).

Table 9-2 Patient Demographics (Primary Analysis Population)

	Periconception	Later First Trimester	Second Trimester	Third Trimester	Overall
Age (years)					
n	195	87	140	62	484
Mean (SD)	29.3 (5.65)	29.2 (5.67)	29.1 (5.91)	28.2 (5.84)	29.1 (5.75)
Median	29.0	28.0	29.0	28.0	29.0
Min, Max	18, 43	19, 44	18, 43	18, 41	18, 44
Height (cm)					
n	195	87	139	62	483
Mean (SD)	162.185 (6.0568)	161.731 (7.1045)	163.401 (6.8693)	162.705 (6.9711)	162.520 (6.6195)
Median	162.200	162.500	162.560	162.580	162.500
Min, Max	142.20, 180.00	143.00, 175.00	144.80, 177.80	149.86, 185.00	142.20, 185.00
Weight (kg)					
n	195	87	140	61	483
Mean (SD)	78.51 (22.752)	76.17 (18.481)	78.10 (20.601)	74.91 (15.458)	77.51 (20.570)
Median	74.40	72.00	75.05	74.80	74.60
Min, Max	38.1, 169.1	46.2, 121.6	44.0, 155.4	44.7, 122.0	38.1, 169.1
BMI (kg/m^2)					
n	195	87	139	61	482
Mean (SD)	29.760 (8.1398)	29.036 (6.5112)	29.334 (7.6445)	28.413 (5.8673)	29.336 (7.4539)
Median	28.140	28.110	28.340	27.160	28.125
Min, Max	15.36, 63.96	18.14, 46.25	17.19, 62.09	17.26, 42.21	15.36, 63.96
Race n (%)					
White	36 (18.5)	15 (17.2)	24 (17.1)	7 (11.3)	82 (16.9)
Black or African American	139 (71.3)	68 (78.2)	107 (76.4)	48 (77.4)	362 (74.8)
Asian	1 (0.5)	1 (1.1)	1 (0.7)	1 (1.6)	4 (0.8)
American Indian or Alaska Native	2 (1.0)	0	2 (1.4)	0	4 (0.8)
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Other	17 (8.7)	3 (3.4)	6 (4.3)	6 (9.7)	32 (6.6)
Ethnicity n (%)					
Hispanic or Latino	35 (17.9)	13 (14.9)	22 (15.7)	6 (9.7)	76 (15.7)
Not Hispanic or Latino	150 (76.9)	70 (80.5)	110 (78.6)	54 (87.1)	384 (79.3)
Not reported	10 (5.1)	3 (3.4)	8 (5.7)	2 (3.2)	23 (4.8)
Unknown	0	1 (1.1)	0	0	1 (0.2)

SD = Standard Deviation, BMI = Body Mass Index
Note: Percentages are based on the number of primary analysis population in each column (N).

The majority of individuals had been HIVpositive for 5 years or more (51.0%) or for 1 to 5 years (24.4%). The majority of patient's worst disease severity of HIV was asymptomatic, acute (primary) HIV or PGL (persistent generalized lymphadenopathy) (66.1%). There were 51.7% of individuals with a VL >200 copies/mL at any time during

the last 12 months and 44.8% who maintained a VL <200 copies/mL. The majority of patient's VL at delivery was <50 copies/mL (57.9%), however it was missing for 144 individuals (29.8%).

The earliest CD4+ T-cell category during this pregnancy was ≥500 cells/μL for 48.8%, 200-499 cells/μL for 33.1%, and <200 cells/μL for 13.8%. At the time of delivery, 35.7% had a CD4+ T-cell count of ≥500 cells/μL, 23.6% had 200-499 cells/μL, 7.6% had <200 cells/μL, and 33.1% had a missing CD4+.

The median Nadir CD4 in patient's history was 336.0 (min, max=1, 1420). Genotypic assays were available for 462/484 individuals. Of the 462 individuals with resistance test results, 12.8% of individuals indicated resistance to NRTIs, 9.3% indicated resistance to NNRTIs, 3.9% indicated resistance to PIs, 2.3% indicated resistance to INSTIs, and 76.2% of individuals were not resistant to NRTIs, NNRTIs, PIs, or INSTIs. Individual's disease characteristics were consistent across all exposure timing categories with the exception of the periconception category for VL >200 copies/mL during the last 12 months (**Table 9-3**).

Table 9-3 Patient Disease Characteristics (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62	Overall N=484
Timing of HIV Diagnosis					
Diagnosed during this pregnancy	3 (1.5)	19 (21.8)	40 (28.6)	24 (38.7)	86 (17.8)
<1 year	5 (2.6)	7 (8.0)	12 (8.6)	2 (3.2)	26 (5.4)
1-5 years	66 (33.8)	15 (17.2)	25 (17.9)	12 (19.4)	118 (24.4)
5 years +	119 (61.0)	46 (52.9)	61 (43.6)	21 (33.9)	247 (51.0)
Unknown	2 (1.0)	0	2 (1.4)	3 (4.8)	7 (1.4)
Worst Disease Severity of HIV					
A. Asymptomatic, acute (primary) HIV or PGL (persistent generalized lymphadenopathy)	128 (65.6)	58 (66.7)	90 (64.3)	44 (71.0)	320 (66.1)
B. Symptomatic, not (A) or (C) conditions	20 (10.3)	12 (13.8)	13 (9.3)	3 (4.8)	48 (9.9)
C. Other AIDS-indicator conditions	3 (1.5)	2 (2.3)	2 (1.4)	1 (1.6)	8 (1.7)
D. CD4 <200 cells/μL	30 (15.4)	11 (12.6)	25 (17.9)	11 (17.7)	77 (15.9)
E. AIDS Defining Illness	9 (4.6)	3 (3.4)	9 (6.4)	1 (1.6)	22 (4.5)
Missing	5 (2.6)	1 (1.1)	1 (0.7)	2 (3.2)	9 (1.9)
Viral Load >200 during the last 12 months[a]					
Yes	61 (31.3)	55 (63.2)	88 (62.9)	46 (74.2)	250 (51.7)
No	125 (64.1)	32 (36.8)	48 (34.3)	12 (19.4)	217 (44.8)
Missing	9 (4.6)	0	4 (2.9)	4 (6.5)	17 (3.5)
Viral Load Categories at Delivery					
<50 copies/mL	112 (57.4)	54 (62.1)	80 (57.1)	34 (54.8)	280 (57.9)
≥50-<200 copies/mL	5 (2.6)	3 (3.4)	9 (6.4)	7 (11.3)	24 (5.0)
≥200 copies/mL	16 (8.2)	6 (6.9)	8 (5.7)	6 (9.7)	36 (7.4)
Missing	62 (31.8)	24 (27.6)	43 (30.7)	15 (24.2)	144 (29.8)

Earliest CD4+ T-cell Categories in this Pregnancy					
<200 cells/µL	19 (9.7)	12 (13.8)	25 (17.9)	11 (17.7)	67 (13.8)
200-499 cells/µL	52 (26.7)	30 (34.5)	52 (37.1)	26 (41.9)	160 (33.1)
≥ 500 cells/µL	113 (57.9)	45 (51.7)	58 (41.4)	20 (32.3)	236 (48.8)
Missing	11 (5.6)	0	5 (3.6)	5 (8.1)	21 (4.3)
CD4+ T-cell Categories at Delivery					
<200 cells/µL	14 (7.2)	8 (9.2)	13 (9.3)	2 (3.2)	37 (7.6)
200-499 cells/µL	38 (19.5)	26 (29.9)	33 (23.6)	17 (27.4)	114 (23.6)
≥ 500 cells/µL	81 (41.5)	29 (33.3)	42 (30.0)	21 (33.9)	173 (35.7)
Missing	62 (31.8)	24 (27.6)	52 (37.1)	22 (35.5)	160 (33.1)
Nadir CD4 in Patient's History					
n	140	59	104	40	343
Mean (SD)	392.2 (273.29)	360.5 (223.17)	379.9 (263.47)	366.9 (224.98)	380.1 (256.18)
Median	336.5	321.0	341.5	318.5	336.0
Min, Max	2, 1142	4, 929	1, 1420	13, 835	1, 1420
Genotypic Assays Indicated Resistance[b]					
NRTIs	28 (14.4)	11 (12.6)	14 (10.0)	9 (14.5)	62 (12.8)
NNRTIs	18 (9.2)	10 (11.5)	9 (6.4)	8 (12.9)	45 (9.3)
PIs	9 (4.6)	4 (4.6)	4 (2.9)	2 (3.2)	19 (3.9)
INSTIs	4 (2.1)	2 (2.3)	4 (2.9)	1 (1.6)	11 (2.3)
None of the above	143 (73.3)	71 (81.6)	113 (80.7)	42 (67.7)	369 (76.2)
Missing	3 (1.5)	3 (3.4)	10 (7.1)	6 (9.7)	22 (4.5)

SD = Standard Deviation
a If a patient has viral load > 200 at least once during the pregnancy, the patient is counted as 'Yes'.
b Individuals can have more than one category.
Note: Percentages are based on the number of primary analysis population in each column (N).

Overall, the median days between LMP and date of first DTG exposure was 71.0 days (min, max=-1942, 513); -414.0 days (min, max=-1942, 55) in periconception, 83.0 days (min, max=57, 110) in later first trimester, 152.0 days (min, max=112, 208) in second trimester, and 236.0 days (min, max=212, 513) in third trimester.

Overall, the median days between date of first DTG exposure to estimated date of delivery (EDD) was 197 days (min, max=-214, 10639); 698.5 days (min, max=241, 10639) in periconception, 210.5 days (min, max=186, 239) in later first trimester, 152.0 days (min, max=94, 183) in second trimester, and 54.0 days (min, max=-214, 79) in third trimester.

Overall, the median GA at time of first DTG exposure was 10.430 weeks (min, max=0.00, 71.29)); 0.000 weeks (min, max=0.00, 5.86) in periconception, 9.860 weeks (min, max=6.00, 13.71) in later first trimester, 18.640 weeks (min, max=14.00, 27.71) in second trimester, and 32.360 weeks (min, max=-28.29, 71.29) in third trimester (Table 9-4).

Table 9-4 Prenatal Information (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62	Overall N=484
Days from LMP to Date of DTG Exposure					
n	67	33	36	13	149
Mean (SD)	-523.1 (530.44)	85.0 (15.10)	154.7 (29.44)	261.1 (79.11)	-156.2 (488.84)
Median	-414.0	83.0	152.0	236.0	71.0
Min, Max	-1942, 55	57, 110	112, 208	212, 513	-1942, 513
Days from Date of DTG Exposure EDD					
n	128	54	104	49	335
Mean (SD)	873.9 (991.58)	210.5 (15.81)	144.3 (26.32)	32.6 (70.97)	417.4 (711.74)
Median	698.5	210.5	152.0	54.0	197.0
Min, Max	241, 10639	186, 239	94, 183	-214, 79	-214, 10639
Gestational Age at Time of DTG Exposure (weeks)					
n	195	87	140	62	484
Mean (SD)	0.504 (1.4087)	10.103 (2.2082)	19.678 (3.8724)	35.442 (10.2961)	12.251 (12.6860)
Median	0.000	9.860	18.640	32.360	10.430
Min, Max	0.00, 5.86	6.00, 13.71	14.00, 27.71	28.29, 71.29	0.00, 71.29

SD = Standard Deviation
Note: Days from LMP (or estimated date of conception) to date of first exposure [the first DTG date – LMP date (or date of conception -14) + 1]
Note: Days from date of first exposure to expected delivery date (EDD) [the EDD date - the first DTG date + 1]
Note: Days from date of first exposure to corrected expected delivery date (CEDD) [the CEDD date - the first DTG date + 1]

Overall, 438 individuals (90.5%) had any prenatal testing performed. The most commonly reported prenatal test was an ultrasound (88.4%) (Table 9-5).

Table 9-5 Prenatal Tests (Primary Analysis Population)

	Periconception N=195 n (%)	Later First Trimester N=87 n (%)	Second Trimester N=140 n (%)	Third Trimester N=62 n (%)	Overall N=484 n (%)
Any Prenatal Tests	174 (89.2)	78 (89.7)	130 (92.9)	56 (90.3)	438 (90.5)
Ultrasound	170 (87.2)	76 (87.4)	129 (92.1)	53 (85.5)	428 (88.4)
MSAFP/serum markers	33 (16.9)	17 (19.5)	33 (23.6)	8 (12.9)	91 (18.8)
Other	27 (13.8)	8 (9.2)	23 (16.4)	7 (11.3)	65 (13.4)
First Trimester Screen	26 (13.3)	5 (5.7)	15 (10.7)	6 (9.7)	52 (10.7)
Cystic Fibrosis Mutation Analysis	15 (7.7)	6 (6.9)	16 (11.4)	6 (9.7)	43 (8.9)
Nuchal Translucency	22 (11.3)	9 (10.3)	7 (5.0)	5 (8.1)	43 (8.9)
Fetal Echo	4 (2.1)	2 (2.3)	3 (2.1)	2 (3.2)	11 (2.3)

Note: Percentages are based on the number of individuals (N). Individuals are counted only once if tests were done multiple times within the same test name.

Obstetrical history is summarized in Table 9-6. Overall, the median number of previous pregnancies was 2.0 (min, max=0,10) and the median number of previous live births was 1.0 (min, max =0,7). The majority of previous live births had a normal delivery (54.5%) or caesarean section (30.4%). Overall, the median number of previous outcomes was 2.0 (min, max=0,10), median previous low birth weights was 0.0 (min, max=0,4), median number of spontaneous abortions was 0.0 (min, max=0,9), median number of premature births was 0.0 (min, max=0,4), median number of previous elective abortions was 0.0 (min, max=0,8), and the median number of previous stillbirths was 0.0 (min, max=0,2). A small population of individuals (1.7%) reported a prior termination due to a birth defect or anomaly or a family history of birth defects (1.4%). In addition, a small population of individuals reported a history of abruption placenta (1.0%), eclampsia (0.6%), or preeclampsia (6.4%).

Table 9-6 Obstetrical History (Primary Analysis Population)

	Periconception N=195 n (%)	Later First Trimester N=87 n (%)	Second Trimester N=140 n (%)	Third Trimester N=62 n (%)	Overall N=484 n (%)
Number of Previous Pregnancies					
0	30 (15.4)	16 (18.4)	22 (15.7)	7 (11.3)	75 (15.5)
1	46 (23.6)	16 (18.4)	33 (23.6)	16 (25.8)	111 (22.9)
2	45 (23.1)	21 (24.1)	29 (20.7)	22 (35.5)	117 (24.2)
3+	74 (37.9)	34 (39.1)	56 (40.0)	17 (27.4)	181 (37.4)
Median (min, max)	2.0 (0, 10)	2.0 (0, 8)	2.0 (0, 7)	2.0 (0, 8)	2.0 (0, 10)
Number of Previous Live Births					
0	44 (22.7)	25 (28.7)	31 (22.3)	12 (19.7)	112 (23.3)
1	74 (38.1)	31 (35.6)	43 (30.9)	22 (36.1)	170 (35.3)
2	37 (19.1)	15 (17.2)	38 (27.3)	16 (26.2)	106 (22.0)
3+	39 (20.1)	16 (18.4)	27 (19.4)	11 (18.0)	93 (19.3)

Median (min, max)	1.0 (0, 7)	1.0 (0, 4)	1.0 (0, 4)	1.0 (0, 5)	1.0 (0, 7)
Type of Delivery for Previous Live Births[a]					
Vaginal	107 (55.2)	44 (50.6)	74 (53.2)	37 (60.7)	262 (54.5)
Forceps	1 (0.5)	2 (2.3)	0	1 (1.6)	4 (0.8)
Cesarean Section	55 (28.4)	30 (34.5)	43 (30.9)	18 (29.5)	146 (30.4)
Number of Previous Pregnancy Outcomes					
Median (min, max)	2.0 (0, 10)	2.0 (0, 8)	2.0 (0, 7)	2.0 (0, 8)	2.0 (0, 10)
Number of Previous Low Birth Weights					
0	175 (91.6)	76 (91.6)	118 (91.5)	56 (94.9)	425 (92.0)
1	14 (7.3)	6 (7.2)	9 (7.0)	2 (3.4)	31 (6.7)
2	1 (0.5)	1 (1.2)	2 (1.6)	1 (1.7)	5 (1.1)
3+	1 (0.5)	0	0	0	1 (0.2)
Median (min, max)	0.0 (0, 4)	0.0 (0, 2)	0.0 (0, 2)	0.0 (0, 2)	0.0 (0, 4)
Number of Previous Spontaneous Abortions					
0	120 (62.2)	61 (73.5)	95 (70.9)	43 (70.5)	319 (67.7)
1	55 (28.5)	15 (18.1)	32 (23.9)	12 (19.7)	114 (24.2)
2	14 (7.3)	4 (4.8)	5 (3.7)	4 (6.6)	27 (5.7)
3+	4 (2.1)	3 (3.6)	2 (1.5)	2 (3.3)	11 (2.3)
Median (min, max)	0.0 (0, 9)	0.0 (0, 5)	0.0 (0, 3)	0.0 (0, 4)	0.0 (0, 9)
Number of Previous Premature Births					
0	157 (81.8)	66 (79.5)	115 (87.1)	57 (93.4)	395 (84.4)
1	25 (13.0)	14 (16.9)	15 (11.4)	2 (3.3)	56 (12.0)
2	8 (4.2)	2 (2.4)	2 (1.5)	2 (3.3)	14 (3.0)
3+	2 (1.0)	1 (1.2)	0	0	3 (0.6)
Median (min, max)	0.0 (0, 4)	0.0 (0, 3)	0.0 (0, 2)	0.0 (0, 2)	0.0 (0, 4)
Number of Previous Elective Abortions					
0	158 (81.9)	58 (69.9)	101 (74.8)	53 (86.9)	370 (78.4)
1	20 (10.4)	16 (19.3)	21 (15.6)	7 (11.5)	64 (13.6)
2	8 (4.1)	4 (4.8)	10 (7.4)	1 (1.6)	23 (4.9)
3+	7 (3.6)	5 (6.0)	3 (2.2)	0	15 (3.2)
Median (min, max)	0 (0, 8)	0 (0, 4)	0 (0, 4)	0 (0, 2)	0 (0, 8)
Number of Previous Still Births					
0	188 (97.9)	80 (97.6)	132 (98.5)	59 (96.7)	459 (97.9)
1	3 (1.6)	2 (2.4)	2 (1.5)	2 (3.3)	9 (1.9)
2	1 (0.5)	0	0	0	1 (0.2)
3+	0	0	0	0	0
Median (min, max)	0.0 (0, 2)	0.0 (0, 1)	0.0 (0, 1)	0.0 (0, 1)	0.0 (0, 2)
Any Prior Terminations due to Birth Defects or Anomalies[b]					
Yes	3 (1.5)	2 (2.3)	3 (2.1)	0	8 (1.7)
No	178 (91.3)	81 (93.1)	124 (88.6)	56 (90.3)	439 (90.7)
Unknown	14 (7.2)	4 (4.6)	13 (9.3)	6 (9.7)	37 (7.6)
Family History of Birth Defects[b]					
Yes	4 (2.1)	1 (1.1)	1 (0.7)	1 (1.6)	7 (1.4)
No	131 (67.2)	63 (72.4)	103 (73.6)	37 (59.7)	334 (69.0)
Unknown	60 (30.8)	23 (26.4)	36 (25.7)	24 (38.7)	143 (29.5)
History of Abruption Placenta[b]					
Yes	2 (1.0)	0	2 (1.4)	1 (1.6)	5 (1.0)
No	193 (99.0)	87 (100)	138 (98.6)	61 (98.4)	479 (99.0)
History of Eclampsia[b]					
Yes	0	1 (1.1)	2 (1.4)	0	3 (0.6)

No	195 (100)	86 (98.9)	138 (98.6)	62 (100)	481 (99.4)
History of Preeclampsia[b]					
Yes	13 (6.7)	5 (5.7)	8 (5.7)	5 (8.1)	31 (6.4)
No	182 (93.3)	82 (94.3)	132 (94.3)	57 (91.9)	453 (93.6)

a Percentages are based on the number of previous live birth.
b Percentages are based on the number of individuals in the Primary Analysis population in each group or overall.

Overall, 71.1% of individuals started any ARV medication after conception; 33.3% of periconception individuals, 94.3% of later first trimester individuals, 97.9% of second trimester individuals, and 96.8% of third trimester individuals. The majority of individuals (50.8%) took TIVICAY or "other" medication (44.6%) (Table 9-7).

Table 9-7 Antiretroviral Therapy (Primary Analysis Population)

	Periconception N=195 n (%)	Later First Trimester N=87 n (%)	Second Trimester N=140 n (%)	Third Trimester N=62 n (%)	Overall N=484 n (%)
Any ARV Medications Started After Conception n (%)	65 (33.3)	82 (94.3)	137 (97.9)	60 (96.8)	344 (71.1)
Dolutegravir (DTG) (TIVICAY)	25 (12.8)	63 (72.4)	106 (75.7)	52 (83.9)	246 (50.8)
Dolutegravir/abacavir sulphate (ABC)/lamivudine (3TC) (TRIUMEQ)	11 (5.6)	15 (17.2)	31 (22.1)	7 (11.3)	64 (13.2)
Dolutegravir/rilpivirine (DTG/RPV) (JULUCA)	0	1 (1.1)	0	0	1 (0.2)
Dolutegravir/lamivudine (DTG/3TC) (DOVATO)	1 (0.5)	1 (1.1)	0	0	2 (0.4)
Other	48 (24.6)	43 (49.4)	83 (59.3)	42 (67.7)	216 (44.6)

Note: Percentages are based on the number of individuals (N).
Note: Patient may take multiple categories of medications. At each category, individuals are counted only once.

Overall, the median gestational age at first DTG exposure was 10.10 (min, max=-277.4, 73.3) weeks; -59.10 (min, max=-277.4, 7.9) weeks in periconception individuals, 11.90 (min, max=8.1, 15.7) weeks in later first trimester individuals, 21.70 (min, max=16.0, 29.7) weeks in second trimester individuals, and 33.70 (min, max=30.3, 73.3) weeks in third trimester individuals. Overall, the median total duration of DTG was 1461.0 (min, max=1, 10613) days; 2071.0 (min, max=1, 10613) days in periconception individuals, 932.0 (min, max=1, 2616) days in later first trimester individuals, 1157.5 (min, max=1, 2920) days in second trimester individuals, and 1061.0 (min, max=1, 3138) days in third

trimester individuals. The majority of individuals (88.0%) had ≥196 days of DTG duration. Overall, 195 (40.3%) of individuals reported DTG discontinuation with the majority of discontinuation reasons being a change in regimen (Table 9-8).

Table 9-8 DTG Treatment Exposure (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62	Overall N=484
Gestational Age at First DTG exposure (weeks)					
n	67	33	36	13	149
Mean (SD)	-74.74 (75.776)	12.13 (2.156)	22.09 (4.206)	37.28 (11.308)	-22.33 (69.832)
Median	-59.10	11.90	21.70	33.70	10.10
Min, Max	-277.4, 7.9	8.1, 15.7	16.0, 29.7	30.3, 73.3	-277.4, 73.3
Total Duration of DTG (days)					
n	195	87	140	62	484
Mean (SD)	1882.6 (1020.21)	1036.7 (753.28)	1162.1 (683.98)	1066.2 (860.89)	1417.5 (946.33)
Median	2071.0	932.0	1157.5	1061.0	1461.0
Min, Max	1, 10613	1, 2616	1, 2920	1, 3138	1, 10613
< 42 Days	6 (3.1)	6 (6.9)	2 (1.4)	8 (12.9)	22 (4.5)
42 -≤ 97 Days	0	2 (2.3)	6 (4.3)	5 (8.1)	13 (2.7)
98 -≤195 Days	3 (1.5)	7 (8.0)	10 (7.1)	3 (4.8)	23 (4.8)
≥196 Days	186 (95.4)	72 (82.8)	122 (87.1)	46 (74.2)	426 (88.0)
Individuals that reported DTG discontinuation	48 (24.6)	36 (41.4)	72 (51.4)	39 (62.9)	195 (40.3)
Reasons for Discontinuation[a]:					
Change in regimen	24	10	33	8	75
Pregnancy	20	6	8	3	37
Resistance/Viral load	6	3	12	9	30
Not previously on therapy	2	9	14	2	27
Side effects	3	3	12	6	24
Safety concerns	15	4	4	0	23
Compliance/adherence issues	9	2	5	5	21
Clinical decision	2	4	4	4	14
Other/Unknown	1	0	6	5	12
Patient decision	3	0	1	4	8
New Diagnosis of HIV	0	0	0	6	6

SD = Standard Deviation
a individuals may have more than one reason for discontinuation. Reasons are counted only once if individuals reported multiple reasons within the same discontinuation reason category.
Note: Percentages are based on the number of individuals (N).
Note: Gestational week at first DTG exposure is calculated as (DTG first exposure date - date of LMP +1)/7.

Note: Total duration of DTG is defined as the number of days that the patient is known to have been exposed to DTG during the study. Days of duration (per trimester) will be calculated separately during each trimester.

Overall, 245 individuals (50.6%) reported any concomitant medication; 112 individuals (23.1%) reported any concomitant medication during the first trimester, 133 individuals (27.5%) reported any concomitant medication during the second trimester, and 145 individuals (30.0%) reported any concomitant medication during the third trimester (Table 9-9). Overall, the most commonly reported concomitant medication was antibacterials for systemic use.

Table 9-9 Concomitant Medication (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62	Overall N=484
Any Concomitant Medications	110 (56.4)	31 (35.6)	76 (54.3)	28 (45.2)	245 (50.6)
Any Concomitant Medications During First Trimester	58 (29.7)	19 (21.8)	30 (21.4)	5 (8.1)	112 (23.1)
Any Concomitant Medications During Second Trimester	60 (30.8)	20 (23.0)	45 (32.1)	8 (12.9)	133 (27.5)
Any Concomitant Medications During Third Trimester	53 (27.2)	23 (26.4)	48 (34.3)	21 (33.9)	145 (30.0)

Note: Percentages are based on the number of individuals (N).
Data Source: Tables 14.1.4.1.1-14.1.4.2.4

Overall, 482 individuals (99.6%) reported any concurrent comorbidities; 418 individuals (86.4%) reported any concurrent comorbidities during the first trimester, 422 individuals (87.2%) reported any concurrent comorbidities during the second trimester, and 431 individuals (89.0%) reported any concurrent comorbidities during the third trimester (Table 9-10).

Table 9-10 Concurrent Comorbidities (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62	Overall N=484
Any Concurrent Comorbidities	195 (100)	87 (100)	139 (99.3)	61 (98.4)	482 (99.6)
Any Concomitant Comorbidities During First Trimester	177 (90.8)	84 (96.6)	113 (80.7)	44 (71.0)	418 (86.4)
Any Concomitant Comorbidities During Second Trimester	163 (83.6)	85 (97.7)	126 (90.0)	48 (77.4)	422 (87.2)
Any Concomitant Comorbidities During Third Trimester	161 (82.6)	83 (95.4)	128 (91.4)	59 (95.2)	431 (89.0)

Note: Percentages are based on the number of individuals (N).
Note: Individuals with diabetes (pregestational or gestation) and those with any infections/conditions prior to or during the pregnancy are presented.
Data Source: Tables 14.1.4.3.1-14.1.4.3.4

9.3 Results of Essential Analyses

Overall, the majority of individuals at each visit had a VL of <50 copies/mL; 38.9% at discontinuation/switching of DTG during pregnancy, 51.0% at the start of pregnancy, 53.5% during the first trimester, 63.5% during the second trimester, 73.2% during the third trimester, and 82.6% at delivery.

Additionally, the majority of individuals at each visit had a VL of <200; 46.0% at discontinuation/switching of DTG during pregnancy, 56.8% at the start of pregnancy, 61.2% during the first trimester, 73.7% during the second trimester, 81.2% during the third trimester, and 89.6% at delivery.

Overall, VL ≥200 was reported in 107/198 individuals (54.0%) at discontinuation/switching of DTG during pregnancy, 134/310 individuals (43.2%) at the start of pregnancy, 110/284 (38.7%) during the first trimester, 103/392 (26.3%) during the second trimester, 78/414 (18.8%) during the third trimester, and 34/327 (10.4%) at delivery (Table 9-11).

An ordinal regression analysis was performed using maternal VL at delivery as the dependent variable and trimester of DTG exposure as the independent variable. Compared to the periconception group, the odds ratio for later first trimester was 0.986 (95% CI 0.675, 1.442), 0.965 (95% CI 0.687, 1.355) for second trimester and 0.648 (95% CI 0.428, 0.981) for third trimester (Table 9-12). This indicates that there is no difference in VL at delivery for individuals that started DTG in either later first trimester or second trimester compared to individuals that started DTG periconception. However, VLs at delivery were higher in individuals that started DTG in the third trimester compared to individuals that started DTG periconception.

Table 9-11 Maternal Viral Load by Visit (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62	Overall N=484
At Discontinuation/Switching of DTG during Pregnancy, n (%)	45	50	67	36	198
<50	28 (62.2)	20 (40.0)	20 (29.9)	9 (25.0)	77 (38.9)
≥50-<200	2 (4.4)	1 (2.0)	8 (11.9)	3 (8.3)	14 (7.1)
≥200-<10,000	6 (13.3)	16 (32.0)	20 (29.9)	11 (30.6)	53 (26.8)
≥10,000-<100,000	6 (13.3)	10 (20.0)	14 (20.9)	9 (25.0)	39 (19.7)
≥100,000	3 (6.7)	3 (6.0)	5 (7.5)	4 (11.1)	15 (7.6)
At Start of Pregnancy, n (%)	143	65	81	21	310
<50	102 (71.3)	26 (40.0)	25 (30.9)	5 (23.8)	158 (51.0)
≥50-<200	6 (4.2)	3 (4.6)	5 (6.2)	4 (19.0)	18 (5.8)
≥200-<10,000	14 (9.8)	17 (26.2)	22 (27.2)	5 (23.8)	58 (18.7)
≥10,000-<100,000	19 (13.3)	16 (24.6)	24 (29.6)	4 (19.0)	63 (20.3)
≥100,000	2 (1.4)	3 (4.6)	5 (6.2)	3 (14.3)	13 (4.2)
During First Trimester, n (%)	138	78	54	14	284
<50	98 (71.0)	32 (41.0)	19 (35.2)	3 (21.4)	152 (53.5)
≥50-<200	8 (5.8)	6 (7.7)	4 (7.4)	4 (28.6)	22 (7.7)
≥200-<10,000	14 (10.1)	21 (26.9)	12 (22.2)	4 (28.6)	51 (18.0)
≥10,000-<100,000	16 (11.6)	14 (17.9)	15 (27.8)	3 (21.4)	48 (16.9)
≥100,000	2 (1.4)	5 (6.4)	4 (7.4)	0	11 (3.9)
During Second Trimester, n (%)	154	79	129	30	392
<50	120 (77.9)	61 (77.2)	54 (41.9)	14 (46.7)	249 (63.5)
≥50-<200	12 (7.8)	6 (7.6)	18 (14.0)	4 (13.3)	40 (10.2)
≥200-<10,000	14 (9.1)	12 (15.2)	30 (23.3)	8 (26.7)	64 (16.3)
≥10,000-<100,000	8 (5.2)	0	20 (15.5)	3 (10.0)	31 (7.9)
≥100,000	0	0	7 (5.4)	1 (3.3)	8 (2.0)
During Third Trimester, n (%)	151	78	129	56	414
<50	118 (78.1)	63 (80.8)	99 (76.7)	23 (41.1)	303 (73.2)
≥50-<200	11 (7.3)	3 (3.8)	14 (10.9)	5 (8.9)	33 (8.0)
≥200-<10,000	12 (7.9)	9 (11.5)	11 (8.5)	15 (26.8)	47 (11.4)
≥10,000-<100,000	8 (5.3)	3 (3.8)	4 (3.1)	11 (19.6)	26 (6.3)
≥100,000	2 (1.3)	0	1 (0.8)	2 (3.6)	5 (1.2)
At Delivery, n (%)	127	63	93	44	327
<50	108 (85.0)	54 (85.7)	76 (81.7)	32 (72.7)	270 (82.6)
≥50-<200	4 (3.1)	3 (4.8)	9 (9.7)	7 (15.9)	23 (7.0)
≥200-<10,000	11 (8.7)	6 (9.5)	7 (7.5)	2 (4.5)	26 (8.0)
≥10,000-<100,000	2 (1.6)	0	1 (1.1)	2 (4.5)	5 (1.5)
≥100,000	2 (1.6)	0	0	1 (2.3)	3 (0.9)

Note: Percentages are based on the number of individuals at each summarization.
Data Source: Tables 14.2.1.1.1

Table 9-12 Maternal Viral Load at Delivery (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62
n	186	87	136	59
Odds Ratio	-	0.986	0.965	0.648
95% Confidence Interval	-	(0.675, 1.442)	(0.687, 1.355)	(0.428, 0.981)

Note: n represents the number of participants included in the model in each category.
Note: The ordinal logistic regression model is using the 5 categories of viral load at delivery as dependent variable and study strata as independent variables.
Note: Odds ratios and 95% confidence intervals are compared to the Periconception group.

Overall, there were 483 individuals with pregnancy outcomes: 195 in periconception individuals, 86 in later first trimester individuals, 140 in second trimester individuals, and 62 in third trimester individuals. Overall, there were 449 (93.0%; 95% CI 90.3, 95.1) live births, 8 (1.7%; 95% CI 0.7, 3.2) stillbirths, 19 (3.9%; 95% CI 2.4, 6.1) spontaneous abortions, and 7 (1.4%; 95% CI 0.6, 3.0) induced abortions (Table 9-13).

Table 9-13 Current Pregnancy Outcomes (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62	Overall N=484
Number of individuals with Pregnancy Outcome(s)	195	86	140	62	483
Live Birth n (%)	171 (87.7)	81 (94.2)	135 (96.4)	62 (100)	449 (93.0)
95% CI	(82.2, 92.0)	(87.0, 98.1)	(91.9, 98.8)	(94.2, 100)	(90.3, 95.1)
Stillbirth n (%)	4 (2.1)	1 (1.2)	3 (2.1)	0	8 (1.7)
95% CI	(0.6, 5.2)	(0, 6.3)	(0.4, 6.1)	(0, 5.8)	(0.7, 3.2)
Spontaneous Abortion n (%)	14 (7.2)	4 (4.7)	1 (0.7)	0	19 (3.9)
95% CI	(4.0, 11.8)	(1.3, 11.5)	(0, 3.9)	(0, 5.8)	(2.4, 6.1)
Induced Abortion n (%)	6 (3.1)	0	1 (0.7)	0	7 (1.4)
95% CI	(1.1, 6.6)	(0, 4.2)	(0, 3.9)	(0, 5.8)	(0.6, 3.0)

CI = Confidence Interval
Note: Percentages are based on the number of individuals with pregnancy outcome(s).
Note: Two-sided 95% confidence intervals are calculated using the exact binomial distribution (Clopper-Pearson method).

Neonatal HIV status (positive vs. negative) was summarized for the infant by study strata and overall. There were 458 live births overall: 178 in periconception, 81 in later first trimester, 137 in second trimester, and 62 in third trimester. The majority of infants (88.6%) were HIV negative; 89.9% of periconception infants, 87.7% in later first trimester infants, 88.3% in second trimester infants, and 87.1% in third trimester infants.

Overall, there were 6 (1.3%) infants that were HIV positive; 1 in periconception, 0 in later first trimester, 3 in second trimester, and 2 in third trimester. Logistic models were applied to analyze the odds ratio between trimesters (using periconception period as reference). The odds ratio for later first trimester was 2.09E-10 (95% CI 0-Inf), 3.9669 (95% CI 0.4076-38.6077) for second trimester, 5.9259 (95% CI 0.5268-66.6550) for third trimester, and 2.3645 (95% CI 0.2824-19.7959) overall (Table 9-14). This indicates that there is no difference between infant HIV status and the start of DTG.

Table 9-14 Infant HIV Status (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62	Overall N=484
Number of Live Birth	178	81	137	62	458
Neonatal HIV Status					
Positive	1 (0.6)	0	3 (2.2)	2 (3.2)	6 (1.3)
Negative	160 (89.9)	71 (87.7)	121 (88.3)	54 (87.1)	406 (88.6)
Missing	17 (9.6)	10 (12.3)	13 (9.5)	6 (9.7)	46 (10.0)
Odds ratio from Logistic Model		2.09E-10	3.9669	5.9259	2.3645
95% CI (vs. Periconception period)		0-Inf	0.4076-38.6077	0.5268-66.6550	0.2824-19.7959

CI = Confidence Interval
Note: Percentages are based on the number of live births.
Note: Logistic model is using neonatal HIV status as dependent variable (HIV infected as 1, HIV uninfected as 0), and trimester as independent variable. Neonatal HIV status from periconception period is used as reference for comparison.

Overall, there were 421 singleton live births without defects: 159 in periconception individuals, 76 in later first trimester individuals, 129 in second trimester individuals, and 57 in third trimester individuals. Overall, there were 65 (15.4%; 95% CI 12.1, 19.3) preterm births, 7 (1.7%; 95% CI 0.7, 3.4) severely preterm births, 56 (13.3%; 95% CI 10.2, 16.9) low birth weight (LBW), 0 (95% CI 0.0, 0.9) very LBW, and 2 (0.5%; 95% CI 0.1, 1.7) extremely LBW. (Table 9-15).

Table 9-15 Current Infant Outcomes (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62	Overall N=484
Number of Individuals with Non-Defect and Singleton Births Infant Outcome(s)	159	76	129	57	421
Preterm Birth n (%)	22 (13.8)	15 (19.7)	23 (17.8)	5 (8.8)	65 (15.4)
95% CI	(8.9, 20.2)	(11.5, 30.5)	(11.7, 25.5)	(2.9, 19.3)	(12.1, 19.3)
Severely Preterm Birth n (%)	1 (0.6)	2 (2.6)	2 (1.6)	2 (3.5)	7 (1.7)
95% CI	(0, 3.5)	(0.3, 9.2)	(0.2, 5.5)	(0.4, 12.1)	(0.7, 3.4)
Low Birth Weight n (%)	17 (10.7)	10 (13.2)	20 (15.5)	9 (15.8)	56 (13.3)
95% CI	(6.4, 16.6)	(6.5, 22.9)	(9.7, 22.9)	(7.5, 27.9)	(10.2, 16.9)
Very Low Birth Weight n (%)	0	0	0	0	0
95% CI	(0, 2.3)	(0, 4.7)	(0, 2.8)	(0, 6.3)	(0, 0.9)
Extremely Low Birth Weight n (%)	1 (0.6)	1 (1.3)	0	0	2 (0.5)
95% CI	(0, 3.5)	(0, 7.1)	(0, 2.8)	(0, 6.3)	(0.1, 1.7)

CI = Confidence Interval
Note: Babies with birth defect are not counted.
Note: Percentages are based on the number of singleton live births without defects.
Note: Preterm birth is birth of live infant at <37 weeks gestation or birth weight <2500 grams if gestational age is not available. Severely preterm birth is birth of live infant at <32 weeks gestation. Low birth weight is birth weight of <2500 grams. Very low birth weight is birth weight of <1500 grams. Extremely low birth weight is birth weight of <1000 grams.
Note: Two-sided 95% confidence intervals are calculated using the exact binomial distribution (Clopper-Pearson method).

Overall, the median gestational age at birth was 38.0 weeks (min, max=24, 45), median birth weight was 3010.00g (min, max=5.8, 4320.0), median length was 49.00cm (min, max=15.5, 62.0), and median head circumference was 33.50cm (min, max=27.0, 48.0). Infant gender was approximately evenly split between male (50.8%) and female (48.0%). The median APGAR score at 5 minutes was 9.0 (min, max=1, 9) and was 9.0 (min, max=3, 10) at 10 minutes. Infant characteristics were consistent across all exposure timing categories (Table 9-16).

Table 9-16 Infant Characteristics (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62	Overall N=484
Number of Individuals with Non-Defect and Singleton Births	159	76	129	57	421
Gestational Age at Birth (weeks)					
n	159	76	129	57	421
Mean (SD)	38.0 (1.94)	37.3 (2.62)	37.8 (2.15)	38.0 (1.95)	37.8 (2.15)
Median	38.0	38.0	38.0	38.0	38.0
Min, Max	24, 45	24, 40	30, 41	30, 41	24, 45
Gender n (%)					
Male	79 (49.7)	41 (53.9)	63 (48.8)	31 (54.4)	214 (50.8)
Female	80 (50.3)	34 (44.7)	65 (50.4)	23 (40.4)	202 (48.0)
Birth Weight (grams)					
n	153	72	124	53	402
Mean (SD)	2956.22 (748.250)	2876.95 (656.041)	2931.13 (775.739)	2890.41 (620.051)	2925.61 (723.755)
Median	3030.00	2977.50	3010.00	2960.00	3010.00
Min, Max	5.8, 4320.0	6.1, 4155.0	6.4, 4210.0	6.1, 4020.0	5.8, 4320.0
Infant Size n (%)[a]					
≤10th percentile	39 (24.5)	21 (27.6)	31 (24.0)	16 (28.1)	107 (25.4)
>10-50th percentile	65 (40.9)	33 (43.4)	49 (38.0)	22 (38.6)	169 (40.1)
>50-90th percentile	43 (27.0)	17 (22.4)	38 (29.5)	13 (22.8)	111 (26.4)
>90th percentile	6 (3.8)	1 (1.3)	6 (4.7)	1 (1.8)	14 (3.3)
Length (cm)					
n	132	58	106	45	341
Mean (SD)	49.18 (3.670)	47.99 (2.914)	48.48 (5.002)	47.13 (8.674)	48.49 (4.955)
Median	49.50	48.00	49.00	49.50	49.00
Min, Max	20.0, 58.0	41.0, 55.0	20.5, 55.9	15.5, 62.0	15.5, 62.0
Head Circumference (cm)					
n	121	58	103	43	325
Mean (SD)	33.59 (1.872)	33.37 (1.618)	33.48 (2.287)	33.47 (1.891)	33.50 (1.968)
Median	33.70	33.25	33.50	33.70	33.50
Min, Max	29.0, 38.1	30.0, 37.5	27.0, 48.0	29.0, 36.5	27.0, 48.0
APGAR Score at 5 Minutes					
n	145	75	122	51	393
Mean (SD)	8.4 (1.13)	8.1 (1.36)	8.3 (1.45)	8.5 (0.88)	8.3 (1.26)
Median	9.0	8.0	9.0	9.0	9.0
Min, Max	2, 9	1, 9	1, 9	5, 9	1, 9
APGAR Score at 10 Minutes					
n	79	53	84	24	240
Mean (SD)	8.7 (0.82)	8.8 (0.78)	8.9 (0.58)	8.9 (0.50)	8.8 (0.71)
Median	9.0	9.0	9.0	9.0	9.0
Min, Max	3, 10	5, 10	5, 10	7, 10	3, 10

SD = Standard Deviations, cm = centimeter

a Infant size is based on the 2006 World Health Organization (WHO) Child Growth Standards used to derive the z-scores for weight-for-age and sex.

Note: Percentages are based on the number of live birth(s).

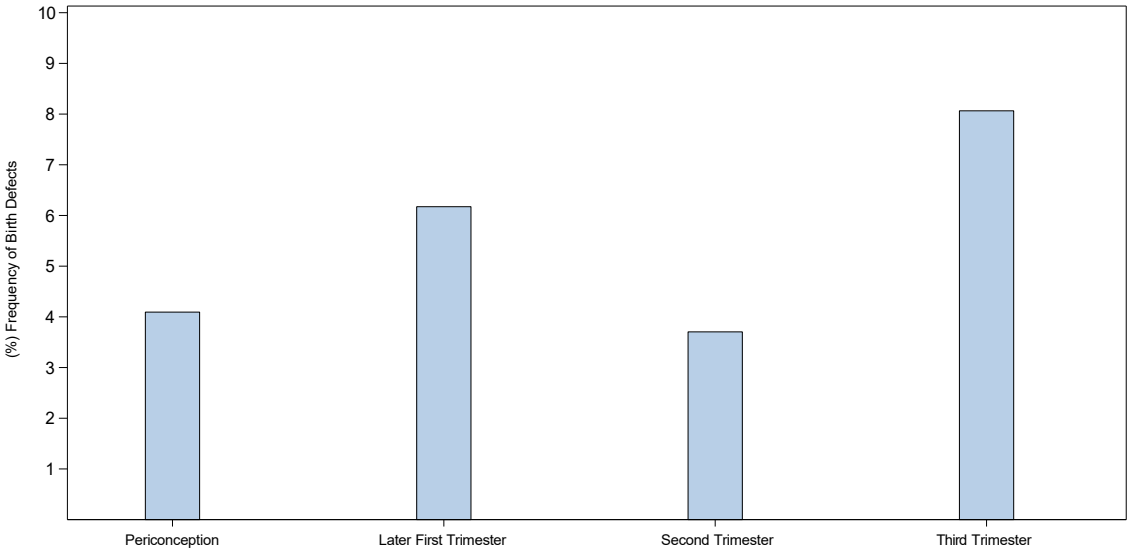
There were 458 live births overall: 178 in periconception individuals, 81 in later first trimester individuals, 137 in second trimester individuals, and 62 in third trimester individuals. There were 23 (5.0%, 95% CI 3.0, 7.1) infants born with at least one birth defect reporting a total of 28 defects: 8 infants (4.5%, 95%CI: 1.8, 7.9) with periconception exposure to DTG, 5 (6.2%, 95% CI: 1.9, 13.0) with exposure in later first trimester, 5 (3.6%, 95% CI: 1.2, 8.1) with exposure in second the trimester, and 5 with exposure (8.1%, 95% CI: 2.7, 17.8) in the third trimester. Overall, there were 2 (0.4%, 95% CI 0.1, 1.5) reported birth defects of polydactyly, 1 (0.2%, 95% CI 0, 1.0) reported birth defect each of ventricular septal defect, hypospadias, and hemangioma, and 23 (5.0%, 95% CI 3.0, 7.1) reported birth defects of "other" (Table 9-17). The 23 "other" birth defects reported included 2 reported birth defects each of patent ductus arteriosus and atrial septal defect, and 1 reported birth defect each of accessory tragus, mild right ventricular hypertrophy, congenital dermal melanocytosis, patent foramen ovale, unspecified anomaly of the ear, left extra mammary nipple, duplicated kidney, dysplastic kidney, hydronephrosis, epispadias, small sacral dimple, macroglossia, micrognathia, hydrocephalus, intraventricular hemorrhage, laryngomalacia, urinary tract dilation, aneurysmal atrial septum, and undescended testicle.

Table 9-17 Birth Defects (Primary Analysis Population)

	Periconception N=195	Later First Trimester N=87	Second Trimester N=140	Third Trimester N=62	Overall N=484
Number of Live Birth	178	81	137	62	458
Any Birth Defects n (%)	8 (4.5)	5 (6.2)	5 (3.6)	5 (8.1)	23 (5.0)
95% CI	(1.8, 7.9)	(1.9, 13.0)	(1.2, 8.1)	(2.7, 17.8)	(3.0, 7.1)
Polydactyly n (%)	1 (0.6)	0	1 (0.7)	0	2 (0.4)
95% CI	(0, 2.8)	(0, 4.2)	(0, 3.9)	(0, 5.8)	(0.1, 1.5)
Ventricular Septal Defect n (%)	1 (0.6)	0	0	0	1 (0.2)
95% CI	(0, 2.8)	(0, 4.2)	(0, 2.6)	(0, 5.8)	(0, 1.1)
Hypospadias n (%)	1 (0.6)	0	0	0	1 (0.2)
95% CI	(0, 2.8)	(0, 4.2)	(0, 2.6)	(0, 5.8)	(0, 1.1)
Hemangiomas n (%)	0	0	0	1 (1.6)	1 (0.2)
95% CI	(0, 1.9)	(0, 4.2)	(0, 2.6)	(0, 8.7)	(0, 1.1)
Other n (%)	8 (4.5)	5 (6.2)	5 (3.6)	5 (8.1)	23 (5.0)
95% CI	(1.8, 7.9)	(1.9, 13.0)	(1.2, 8.1)	(2.7, 17.8)	(3.0, 7.1)

CI = Confidence Interval
Note: Percentages are based on the number of live birth(s).
Note: Two-sided 95% confidence intervals are calculated using the exact binomial distribution (Clopper-Pearson method).
Note: Birth defects can be counted in more than one category.

Figure 9-1 Birth Defects by Gestational Age at Exposure in Weeks



Note: Percentages of birth defects are based on the number of infants who have the birth defect events in Primary Analysis Population. The denominator is the number of infants with live birth.

9.4 Exploratory Analyses

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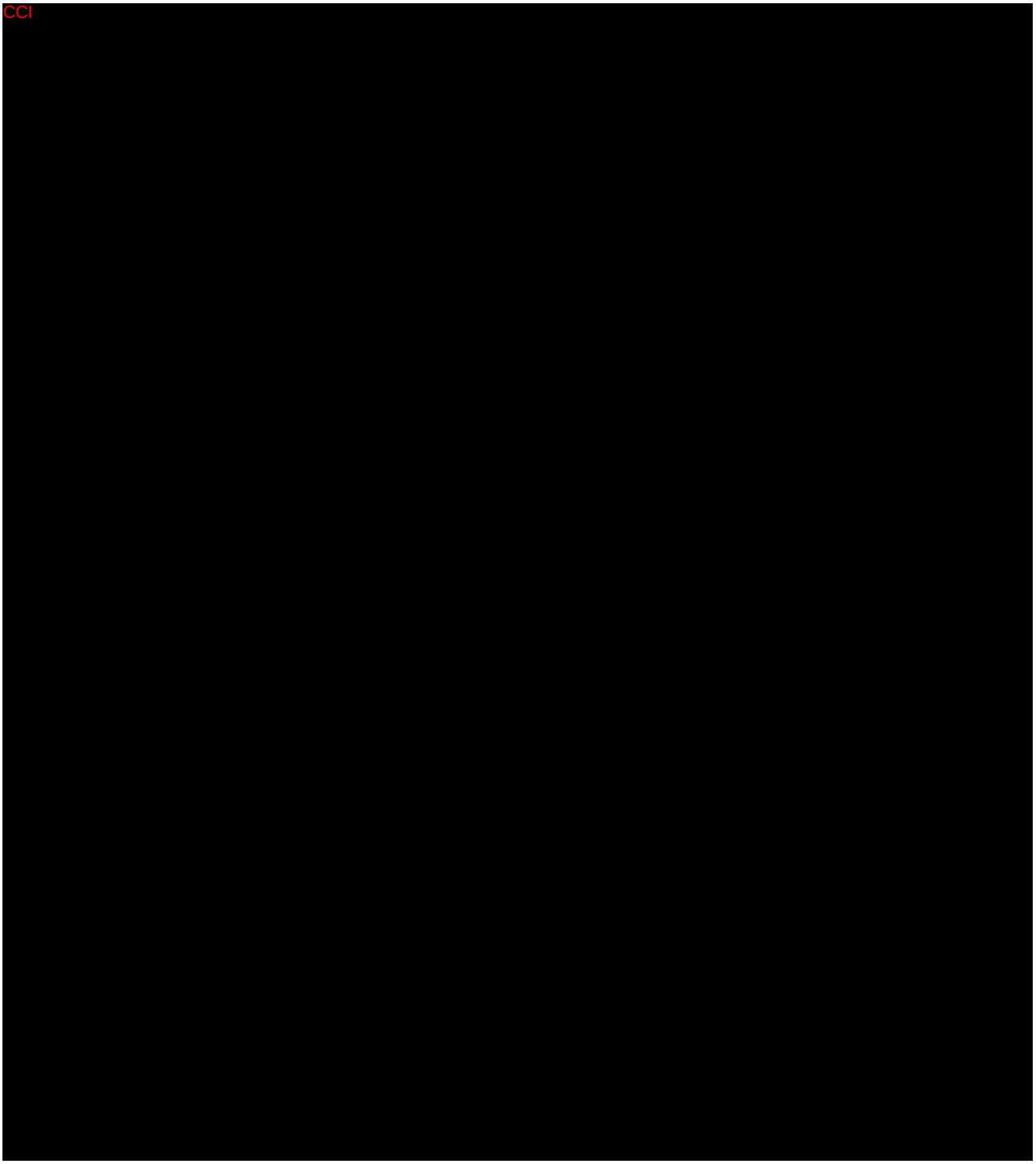


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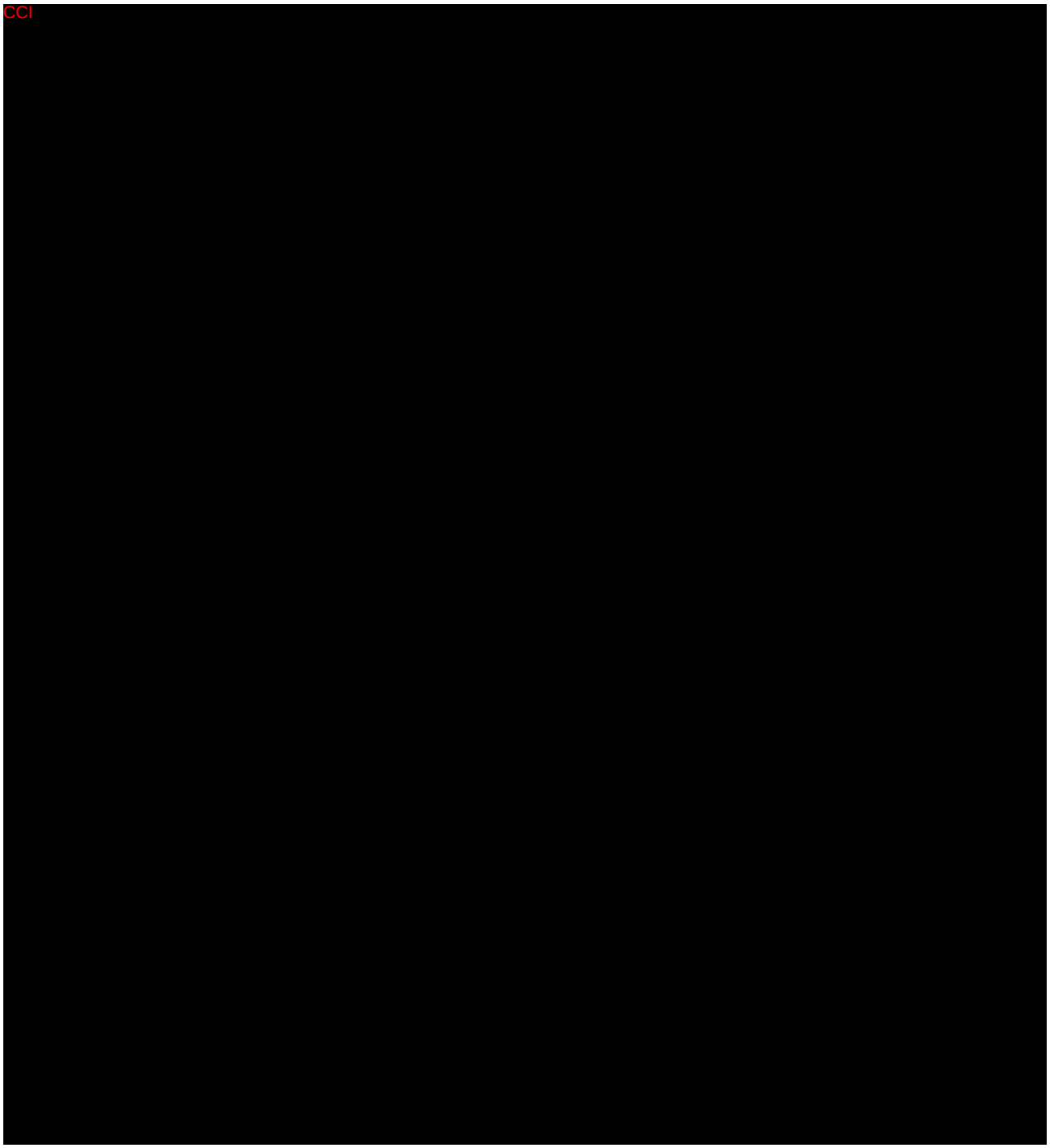

9.5 Ad-Hoc Analyses

Overall, 49.2% of individuals took any antiviral medication before conception; 89.2% of periconception individuals, 26.4% of later first trimester individuals, 20.7% of second trimester individuals, and 19.4% of third trimester individuals. The majority of individuals took “other” medication (26.4%) or TIVICAY (22.1%) (Table 9-23).

Table 9-23 Previous Antiviral Therapy Taken by Treatment Experienced (Primary Analysis Population)

	Periconception N=195 n (%)	Later First Trimester N=87 n (%)	Second Trimester N=140 n (%)	Third Trimester N=62 n (%)	Overall N=484 n (%)
Any Antiviral Medications Taken Before Conception	174 (89.2)	23 (26.4)	29 (20.7)	12 (19.4)	238 (49.2)
Dolutegravir (DTG) (TIVICAY)	95 (48.7)	6 (6.9)	4 (2.9)	2 (3.2)	107 (22.1)
Dolutegravir/abacavir sulphate (ABC)/lamivudine (3TC) (TRIUMEQ)	75 (38.5)	3 (3.4)	3 (2.1)	1 (1.6)	82 (16.9)
Dolutegravir/rilpivirine (DTG/RPV) (JULUCA)	1 (0.5)	0	0	0	1 (0.2)
Dolutegravir/lamivudine (DTG/3TC) (DOVATO)	3 (1.5)	0	0	1 (1.6)	4 (0.8)
Other	76 (39.0)	18 (20.7)	26 (18.6)	8 (12.9)	128 (26.4)

Note: Percentages are based on the number of individuals (N).
Note: Patient may take multiple categories of medications. At each category, individuals are counted only once.

Overall, 97.7% of individuals took any antiviral medication before or after conception; 97.4% of periconception individuals, 96.6% of later first trimester individuals, 97.9% of second trimester individuals, and 100% of third trimester individuals. The majority of individuals took TIVICAY (68.8%) or TRIUMEQ (28.5%) (Table 9-24).

Table 9-24 DTG Antiviral Therapy Taken Before or After Conception (Primary Analysis Population)

	Periconception N=195 n (%)	Later First Trimester N=87 n (%)	Second Trimester N=140 n (%)	Third Trimester N=62 n (%)	Overall N=484 n (%)
Any Antiviral Medications Taken Before or after Conception	190 (97.4)	84 (96.6)	137 (97.9)	62 (100)	473 (97.7)
Dolutegravir (DTG) (TIVICAY)	109 (55.9)	66 (75.9)	106 (75.7)	52 (83.9)	333 (68.8)
Dolutegravir/abacavir sulphate (ABC)/lamivudine (3TC) (TRIUMEQ)	82 (42.1)	16 (18.4)	32 (22.9)	8 (12.9)	138 (28.5)
Dolutegravir/rilpivirine (DTG/RPV) (JULUCA)	1 (0.5)	1 (1.1)	0	0	2 (0.4)
Dolutegravir/lamivudine (DTG/3TC) (DOVATO)	4 (2.1)	1 (1.1)	0	1 (1.6)	6 (1.2)

Note: Percentages are based on the number of individuals (N).
Note: Patient may take multiple categories of medications. At each category, individuals are counted only once.

The majority of individuals (89.2%) in the periconception exposure group were treatment experienced. Over 90% of individuals in later first trimester, second trimester and third trimester were treatment naïve (Table 9-25).

Table 9-25 Exposure to DTG Stratified by Treatment Naïve vs Treatment Experienced (Primary Analysis Population)

	Periconception N=195 n (%)	Later First Trimester N=87 n (%)	Second Trimester N=140 n (%)	Third Trimester N=62 n (%)	Overall N=484 n (%)
Treatment Naive	55 (28.2)	79 (90.8)	131 (93.6)	60 (96.8)	325 (67.1)
Treatment Experienced	174 (89.2)	23 (26.4)	29 (20.7)	12 (19.4)	238 (49.2)

Note: Percentages are based on the number of individuals (N).

There were 6 (1.3%) infants diagnosed with HIV; 1 in the periconception exposure group, 3 in the second trimester, and 2 in the third trimester. The mother of the infant with HIV from the periconception exposure group was treatment experienced (TRIUMEQ). Four mothers were treatment naive and initiated treatment during pregnancy (2 each from the second and third trimester). Antiviral DTG was used with "other" in 3 mothers (0.7%) and "other antibiotics" in 1 mother (0.2%). The VL at

delivery was <50 copies/mL for 3 mothers (0.7%), ≥200-<10,000 copies/mL for 1 mother (0.2%) and was unknown for the other 2 mothers (Table 9-26).

Table 9-26 Infant HIV Status as Positive (Primary Analysis Population)

	Periconception N=171 n (%)	Later First Trimester N=81 n (%)	Second Trimester N=135 n (%)	Third Trimester N=62 n (%)	Overall N=449 n (%)
Number of Live Birth	178	81	137	62	458
Neonatal with HIV Positive	1 (0.6)	0	3 (2.2)	2 (3.2)	6 (1.3)
Mothers					
Treatment Experienced	1 (0.6)	0	0	0	1 (0.2)
Treatment Naive	0	0	2 (1.5)	2 (3.2)	4 (0.9)
Antiviral Therapy for Treatment Experienced Mothers					
Dolutegravir/abacavir sulphate (ABC)/lamivudine (3TC) (TRIUMEQ)	1 (0.6)	0	0	0	1 (0.2)
Antiviral DTG Used with:					
Other	1 (0.6)	0	2 (1.5)	0	3 (0.7)
Other Antibiotics	0	0	0	1 (1.6)	1 (0.2)
VL Load at Delivery					
<50 copies/mL	1 (0.6)	0	2 (1.5)	0	3 (0.7)
≥200-<10,000 copies/mL	0	0	0	1 (1.6)	1 (0.2)

Note: Percentages are based on the number of individuals (N).

9.6 Adverse Events/Adverse Reactions

Overall, there were 58 (12.0%) maternal AEs (see Listing 16.2.7.1 in Appendix); 27 (13.8%) in periconception individuals, (11.5%) in later first trimester, 17 (12.1%) in second trimester, and 10 (6.5%) in third trimester individuals. Overall, the majority of AEs were mild in severity (5.4%). Overall, the majority of maternal AEs were considered to be caused by pregnancy (5.8%).

Overall, there were 14 (2.9%) maternal AEs suspected to be related to DTG, or where causality was reported as unknown by the site (see Listing 16.2.7.2 in Appendix); 8 (4.1%) in periconception individuals, 0 in later first trimester, 6 (4.3%) in second trimester, and 0 in third trimester individuals. Maternal AEs suspected to be related to DTG included preterm/premature rupture of membrane, post-partum hemorrhage, vomiting, nausea, dizziness/giddiness/palpitations, headache, vaginal infection, thrombocytopenia, preterm labor, depression and anemia. Causality was reported by the site as 'related' to DTG in only 4 of these cases (PTs of Vomiting, Nausea x 2, headache).

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Table 9-27 Overall Summary of AEs (Primary Analysis Population)

	Periconception N=195 n (%)	Later First Trimester N=87 n (%)	Second Trimester N=140 n (%)	Third Trimester N=62 n (%)	Overall N=484 n (%)
Any Maternal AEs	27 (13.8)	10 (11.5)	17 (12.1)	4 (6.5)	58 (12.0)
Any Maternal AEs by Severity					
Mild	11 (5.6)	2 (2.3)	11 (7.9)	2 (3.2)	26 (5.4)
Moderate	5 (2.6)	5 (5.7)	4 (2.9)	2 (3.2)	16 (3.3)
Severe	4 (2.1)	1 (1.1)	0	1 (1.6)	6 (1.2)
Unknown	11 (5.6)	4 (4.6)	3 (2.1)	0	18 (3.7)
Any Maternal AEs by Cause					
None	5 (2.6)	2 (2.3)	2 (1.4)	0	9 (1.9)
Underlying Disease	2 (1.0)	2 (2.3)	1 (0.7)	0	5 (1.0)
Concomitant Medications	1 (0.5)	0	0	1 (1.6)	2 (0.4)
Pregnancy	12 (6.2)	5 (5.7)	10 (7.1)	1 (1.6)	28 (5.8)
Unknown	7 (3.6)	2 (2.3)	4 (2.9)	1 (1.6)	14 (2.9)
Other	5 (2.6)	1 (1.1)	2 (1.4)	2 (3.2)	10 (2.1)
Any Maternal AEs Suspected to be Related to DTG or considered unknown causality by the site	8 (4.1)	0	6 (4.3)	0	14 (2.9)

AE = Adverse Events
Note: Percentages are based on the number of individuals in primary analysis population.
Note: AEs are considered as DTG related if the relationship is reported as 'Yes', 'Unknown' or missing.
Note: All counts represent the number of individuals (mothers). Individuals are counted only once if experiencing multiple events in the same category.

Overall, there were 21 (4.3%) infant AEs (see Listing 16.2.7.3 in Appendix); 7 (3.6%) in periconception individuals, 9 (10.3%) in later first trimester, 3 (2.1%) in second trimester, and 2 (3.2%) in third trimester individuals. Overall, the majority of infant AEs were pregnancy, puerperium and perinatal conditions (2.1%) (Table 9-36). Overall, 1.0% of infant AEs were mild, 0.8% were moderate, 1.7% were severe, and 0.8% were unknown (Table 9-37).

Table 9-36 Infant AEs (Primary Analysis Population)

Organ System	Periconception N=195 n (%)	Later First Trimester N=87 n (%)	Second Trimester N=140 n (%)	Third Trimester N=62 n (%)	Overall N=484 n (%)
Any Infant AEs	7 (3.6)	9 (10.3)	3 (2.1)	2 (3.2)	21 (4.3)
Pregnancy, puerperium and perinatal conditions	3 (1.5)	4 (4.6)	3 (2.1)	0	10 (2.1)
Psychiatric disorders	2 (1.0)	1 (1.1)	0	0	3 (0.6)
Respiratory, thoracic and mediastinal disorders	1 (0.5)	1 (1.1)	0	0	2 (0.4)
Blood and lymphatic system disorders	0	1 (1.1)	0	0	1 (0.2)
Cardiac disorders	0	1 (1.1)	0	0	1 (0.2)
Ear and labyrinth disorders	1 (0.5)	0	0	0	1 (0.2)
Gastrointestinal disorders	0	0	0	1 (1.6)	1 (0.2)

General disorders and administration site conditions	0	0	0	1 (1.6)	1 (0.2)
Investigations	0	1 (1.1)	0	0	1 (0.2)
Surgical and medical procedures	0	1 (1.1)	0	0	1 (0.2)

AE = Adverse Events
Note: Percentages are based on the number of individuals in primary analysis population.
Note: Adverse events are coded using MedDRA version 22.1.
Note: Patient are counted only once at each summarization.

Table 9-37 Infant AEs by Maximum Severity (Primary Analysis Population)

	Periconception N=195 n (%)	Later First Trimester N=87 n (%)	Second Trimester N=140 n (%)	Third Trimester N=62 n (%)	Overall N=484 n (%)
Any Infant AEs	7 (3.6)	9 (10.3)	3 (2.1)	2 (3.2)	21 (4.3)
Mild	2 (1.0)	2 (2.3)	0	1 (1.6)	5 (1.0)
Moderate	1 (0.5)	3 (3.4)	0	0	4 (0.8)
Severe	3 (1.5)	1 (1.1)	3 (2.1)	1 (1.6)	8 (1.7)
Unknown	1 (0.5)	3 (3.4)	0	0	4 (0.8)

AE = Adverse Events
Note: Percentages are based on the number of individuals in primary analysis population.
Note: Adverse events are coded using MedDRA version 22.1.
Note: Patient will be counted only once if experiencing multiple events in the same System Organ Class/Preferred Term by the maximum severity. Missing severity will be counted as a 'Severe' event.

Overall, there were 14 (2.9%) infant AEs suspected to be related to DTG, or where causal relationship was unknown (see Listing 16.2.7.4 in Appendix); 7 (3.6%) in periconception individuals, 5 (5.7%) in later first trimester, 2 (1.4%) in second trimester, and 0 in third trimester individuals. Infant DTG AEs suspected to be related (or where causal relationship was unknown) to DTG included autism spectrum disorder, missed abortion, spontaneous abortion, intrauterine fetal death, transient tachypnea, hearing loss, intrauterine growth restriction, intrauterine fetal demise, hydrops fetalis, fetal anemia, supraventricular tachycardia, and stillbirth. Of these, none were reported as ‘related’ to DTG at site, but rather the site reported the causal relationship to DTG as ‘unknown’. Overall, the majority of infant AEs suspected to be related to DTG (or where causal relationship was unknown) were pregnancy, puerperium and perinatal conditions (1.7%) (Table 9-38). Overall, 0.6% of infant AEs suspected to be related to DTG (or where causal relationship was unknown) were mild, 0.4% were moderate, 1.2% were severe, and 0.6% were unknown (Table 9-39).

Table 9-38 Infant AEs Suspected to be Related to DTG (or where causal relationship was unknown) (Primary Analysis Population)

Organ System	Periconception N=195 n (%)	Later First Trimester N=87 n (%)	Second Trimester N=140 n (%)	Third Trimester N=62 n (%)	Overall N=484 n (%)
Any Infant AEs suspected to be related to DTG	7 (3.6)	5 (5.7)	2 (1.4)	0	14 (2.9)
Pregnancy, puerperium and perinatal conditions	3 (1.5)	3 (3.4)	2 (1.4)	0	8 (1.7)
Psychiatric disorders	2 (1.0)	1 (1.1)	0	0	3 (0.6)
Blood and lymphatic system disorders	0	1 (1.1)	0	0	1 (0.2)
Cardiac disorders	0	1 (1.1)	0	0	1 (0.2)
Ear and labyrinth disorders	1 (0.5)	0	0	0	1 (0.2)
Respiratory, thoracic and mediastinal disorders	1 (0.5)	0	0	0	1 (0.2)

AE = Adverse Events
Note: Percentages are based on the number of individuals in primary analysis population.
Note: Adverse events are coded using MedDRA version 22.1.
Note: Patient are counted only once at each summarization.

Table 9-39 Infant AEs Suspected to be Related to DTG (or where causal relationship was unknown) by Maximum Severity (Primary Analysis Population)

	Periconception N=195 n (%)	Later First Trimester N=87 n (%)	Second Trimester N=140 n (%)	Third Trimester N=62 n (%)	Overall N=484 n (%)
Any Infant AEs suspected to be related to DTG	7 (3.6)	5 (5.7)	2 (1.4)	0	14 (2.9)
Mild	2 (1.0)	1 (1.1)	0	0	3 (0.6)
Moderate	1 (0.5)	1 (1.1)	0	0	2 (0.4)
Severe	3 (1.5)	1 (1.1)	2 (1.4)	0	6 (1.2)
Unknown	1 (0.5)	2 (2.3)	0	0	3 (0.6)

AE = Adverse Events
Note: Percentages are based on the number of individuals in primary analysis population.
Note: Adverse events are coded using MedDRA version 22.1.
Note: Patient will be counted only once if experiencing multiple events in the same System Organ Class/Preferred Term by the maximum severity. Missing severity will be counted as a 'Severe' event.

10 DISCUSSION

10.1 Results

A total of 572 individuals were enrolled with 484 individuals exposed to DTG that were included in the primary analysis (195 were exposed periconception, 87 exposed later in the first trimester, 140 exposed in the second trimester, and 62 exposed in the third trimester).

Overall, the median gestational age at first DTG exposure was 10.10 (min, max=-277.4, 73.3) weeks. Overall, the median total duration of DTG was 1461.0 (min, max=1, 10613) days. The majority of individuals (88.0%) had ≥196 days of DTG duration. Overall, 195 (40.3%) individuals reported DTG discontinuation with the majority of discontinuation reasons being a change in regimen. The majority of these discontinuations took place between 2018 and 2020, indicating this may be due physician concern around the potential risk of neural tube defects.

Overall, there were 483 individuals with pregnancy outcomes: 195 in periconception individuals, 86 in later first trimester individuals, 140 in second trimester individuals, and 62 in third trimester individuals. Overall, there were 449 (93.0%; 95% CI 90.3, 95.1) live births, 8 (1.7%; 95% CI 0.7, 3.2) stillbirths, 19 (3.9%; 95% CI 2.4, 6.1) spontaneous abortions, and 7 (1.4%; 95% CI 0.6, 3.0) induced abortions.

Out of the 458 live births overall (178 in periconception individuals, 81 in later first trimester individuals, 137 in second trimester individuals, and 62 in third trimester individuals), there were 23 (5.0%) infants reporting a total of 28 birth defects overall (8 infants in periconception individuals, 5 in later first trimester individuals, 5 in second trimester individuals, and 5 in third trimester individuals), which aligns with low birth defect prevalence from the APR data. In the published January 2023 data of the APR, for first trimester DTG exposures overall, the birth defect prevalence was 3.1% (24 defects/783 live births, 95% CI 2.0%, 4.5%) and for second/third trimester DTG exposures overall, the birth defect prevalence was 3.3% (29 defects/874 live births, 95% CI 2.2%, 4.7%), which is similar to the APR overall prevalence of 2.9 birth defects per 100 live births (95% CI: 2.7 - 3.2) [APR 2023].

Overall, there were 2 (0.4%) reported birth defects of polydactyly, 1 (0.2%) reported birth defect of each ventricular septal defect, hypospadias, and hemangioma, and 23 (5.0%) reported birth defects of "other." The 23 "other" birth defects reported included 2 reported birth defects each of patent ductus arteriosus and atrial septal defect, and 1 reported birth defect each of accessory tragus, mild right ventricular hypertrophy, congenital dermal melanocytosis, patent foramen ovale, unspecified anomaly of the ear, left extra mammary nipple, duplicated kidney, dysplastic kidney, hydronephrosis, epispadias, small sacral dimple, macroglossia, micrognathia, hydrocephalus, intraventricular hemorrhage, laryngomalacia, urinary tract dilation, aneurysmal atrial septum, and undescended testicle. No neural tube defects were reported, which aligns with the comparable prevalence of neural tube defects in individuals that were exposed to DTG-containing regimens at the time of conception to non-DTG ARV exposed regimen, as reported in updates from the Tsepamo study [Zash 2022].

Overall, there were 421 singleton live births without defects: 159 in periconception

individuals, 76 in later first trimester individuals, 129 in second trimester individuals, and 57 in third trimester individuals. Overall, infant outcomes included 65 (15.4%) preterm births, 7 (1.7%) severely preterm births, 56 (13.3%) LBW (<2500 g), 0 (0%) very LBW (<1500 g), and 2 (0.5%) extremely LBW (<1000 g).

Overall, the majority of individuals at each visit had a viral load of <50; 38.9% at discontinuation/switching of DTG during pregnancy, 51.0% at the start of pregnancy, 53.5% during the first trimester, 63.5% during the second trimester, 73.2% during the third trimester, and 82.6% at delivery. Additionally, the majority of individuals at each visit had a viral load of <200; 46.0% at discontinuation/switching of DTG during pregnancy, 56.8% at the start of pregnancy, 61.2% during the first trimester, 73.7% during the second trimester, 81.2% during the third trimester, and 89.6% at delivery.

The majority of infants (88.6%) were HIV negative; 89.9% of periconception individuals, 87.7% in later first trimester individuals, 88.3% in second trimester individuals, and 87.1% in third trimester individuals. Overall, there were 6 (1.3%) infants that were HIV positive; 1 in periconception individuals, 0 in later first trimester individuals, 3 in second trimester individuals, and 2 in third trimester individuals.

Overall, there were 58 (12.0%) maternal AEs; the majority were mild in severity (5.4%) and were considered to be caused by pregnancy (5.8%). Overall, there were 14 (2.9%) maternal cases with AEs where causal relationship was considered 'related' to DTG, or where the causal relationship was 'unknown'. The sites reported 4 of these cases as related to DTG (PTs of Vomiting, Nausea x2, headache), while the remainder were reported as causality unknown . Overall, the majority of maternal AEs were pregnancy, puerperium and perinatal conditions (5.2%) and infections and infestations (2.5%). Overall, 4.1% of maternal AEs were mild, 2.9% were moderate, 1.2% were severe, and 3.7% were unknowns. AEs were considered related in 14 infants, but none of these were reported as related by the site. Causal relationship to DTG was 'unknown' in all infant AEs. Review of the reported adverse events in mothers and infants has not identified any new safety issues.

11. CONCLUSIONS

After DTG exposure during conception and all trimesters of pregnancy, the majority of pregnancies resulted in live births (93.0%) with low rates of stillbirths (1.7%), spontaneous abortions (3.9%), and induced abortions (1.4%). While the rate seen for stillbirth is higher than what is reported in the general population in the US, the rate is similar to what is reported by the APR for women exposed to DTG during pregnancy (1.2%) and is lower than what is reported in the HIV population in the US (3.9%) [Brocklehurst and French]. Similarly, the rates of spontaneous abortion are comparable to the rates reported by the APR for women exposed to DTG during pregnancy (4.0%) and in the HIV population in the US (4.1%) [Brocklehurst and French]. Overall, infant outcomes included 65 (15.4%) preterm births, 7 (1.7%) severely preterm births, 56 (13.3%) LBW (<2500 g), 0 (0%) very LBW (<1500 g), and 2 (0.5%) extremely LBW (<1000 g). While the rate of preterm birth is higher than what is reported in the general population in the US, the proportion of infants born preterm and LBW were broadly consistent with incident rates reported in the United States for individuals living with HIV [Watts 2013 and Jao 2017]. The majority of patient's VL at delivery was <50 copies/mL (57.9%), with 10.4% of patient's VL ≥200 copies/mL. There were also low rates of birth

defects (5.0%), no cases of NTD and perinatal HIV transmission (1.3%), demonstrating that DTG continues to be safe and effective for use during pregnancy. In comparison, the birth defect rates reported by MACDP and TBDR are 2.7% and 4.2% respectively, and the rate of vertical transmission seen in the PHACS SMARTT study in the US was 0.5% [Jao 2017]. While a vast majority of individuals achieved virologic suppression by delivery while on DTG (82.6%), close monitoring of adherence and viral load is needed to further reduce perinatal HIV transmission.

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Note: The poster available online presents updated information compared with the published abstract.

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APPENDICES

Listings

Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Periconception

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Preterm premature rupture of membrane	Maternal	PPD 2017/ 2017	Unknown	Unknown	Other: Incompetent cervix	Medications started
	post-partum hemorrhage	Maternal	2018/ 2018	Unknown	Unknown	Pregnancy	Other: post-partum blood transfusion
	PREECLAMPSIA	Maternal	2019/ 2019	Severe	No	Underlying disease	Medications started
	miscarriage	Maternal	2020/ 2020	Unknown	No	None	Other: Patient with early miscarriage. Patient has a personal history of miscarriage. Underwent D&C
	miscarriage	Maternal	2019/ 2019	Unknown	No	None	Medications started
	miscarriage	Maternal	2018/ 2018	Unknown	No	Other: advanced maternal age, personal history of	None

[1] W=White, B=Black or African American, A=Asian, I=American Indian or Alaska Native, P=Native Hawaiian or Other Pacific Islander, O=Other.

Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Periconception

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	cholestasis of pregnancy	Maternal	PPD 2018/ 2018	Mild	No	Pregnancy	Medications started
	miscarriage	Maternal	2018/ 2018	Unknown	No	Unknown	Other: D&C
	ruptured ectopic pregnancy	Maternal	2018/ 2018	Severe	No	Pregnancy	Other: laparoscopic removal of ectopic pregnancy
	hypokalemia	Maternal	2017/ 2017	Mild	No	Unknown	Medications started
	miscarriage	Maternal	2017/ 2017	Unknown	No	None	Medications started
	miscarriage	Maternal	2017/ 2017	Unknown	No	None	Medications started
	miscarriage	Maternal	2015/ 2015	Unknown	No	Pregnancy	Other: D&C
	vomitting	Maternal	2015/ 2016	Mild	Yes	Concomitant medications	Medications started

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Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Periconception

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	miscarriage	Maternal	PPD 2021/ 2021	Mild	No	Pregnancy	None
	nausea	Maternal	2020/	Mild	Yes	Pregnancy	Medications started
	sepsis	Maternal	2020/ 2020	Moderate	No	Underlying disease	Medications started
	sepsis	Maternal	2021/ 2021	Moderate	No	Underlying disease	Medications started
	nausea	Maternal	2021/	Mild	No	Pregnancy	Medications started
	pruritis of hands and feet	Maternal	2021/ 2021	Mild	No	Unknown	None
	gestational hypertension	Maternal	2020/ 2020	Mild	No	Pregnancy	Other: induced 12/21/20
	bacterial vaginosis	Maternal	2019/ 2019	Mild	No	None	Medications started
	Nausea	Maternal	2020/ 2020	Mild	No	Pregnancy	Other: Didn't start ART meds immediately due to nausea

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Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Periconception

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Dizziness, giddiness, and palpitations	Maternal	PPD 2020/ 2020	Unknown	Unknown	Unknown	Other: Unknown. Was at different hospital ED department
	Anemia	Maternal	2020/	Unknown	Unknown	Unknown	Other: Unknown. Was at different hospital ED department
	Cough with rib pain	Maternal	2018/ 2018	Mild	No	Unknown	None
	headache	Maternal	2018/ 2018	Moderate	Unknown	Other: Was also complaining of blurry vision and	None
	Miscarriage	Maternal	2015/ 2015	Unknown	No	Other: Past Medical History of Endometriosis	Other: D&C
	vaginal discharge	Maternal	2018/ 2018	Moderate	No	Pregnancy	Medications started
	Left calf edema with mild cellulitis	Maternal	2018/ 2018	Moderate	No	Unknown	Medications started

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Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Periconception

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Headache, high blood pressure and visual disturbance	Maternal	PPD 2018/ 2018	Moderate	No	Pregnancy	Medications started
	Postpartum Hemorrhage	Maternal	2018/ 2018	Severe	No	Unknown	Other: TAH
	Postpartum Cardiomyopathy	Maternal	2018/ 2018	Severe	No	Unknown	Medications started
	Wound Infection and pelvic abscess	Maternal	2018/ 2018	Severe	No	Unknown	Medications started
	Vaginal Infection	Maternal	2017/ 2017	Moderate	Unknown	Unknown	Medications started
	thrombocytopenia	Maternal	2019/	Mild	Unknown	Pregnancy	None
	Endometritis	Maternal	2019/ 2019	Severe	No	Other: Retained Products of Conception s/p Stillb	Medications started

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Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Later First Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Preeclampsia with severe features	Maternal	PPD 2020/ 2020	Severe	No	Pregnancy	Other: Delivery, antihypertensive medications
	miscarriage	Maternal	2019/ 2019	Unknown	No	Other: chorioamnionitis	Other: patient delivered nonviable fetus
	miscarriage, septic abortion	Maternal	2019/ 2019	Unknown	No	Unknown	Other: patient underwent D&C, was treated in ICU
	miscarriage	Maternal	2020/ 2020	Unknown	No	Unknown	None
	cystitis	Maternal	2017/ 2017	Moderate	No	Pregnancy	Medications started
	Covid 19	Maternal	2020/	Unknown	No	None	None
	Nausea	Maternal	2021/ 2021	Moderate	No	Pregnancy	None

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Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Later First Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Emesis	Maternal	PPD 2017/ 2017	Mild	No	Pregnancy	None
	Nausea	Maternal	2017/ 2017	Moderate	No	Pregnancy	Medications started
	thrombocytopenia	Maternal	2017/ 2017	Moderate	No	Pregnancy	Medications started
	transaminitis	Maternal	2017/ 2017	Moderate	No	Underlying disease	Medications started
	Bacterial vaginosis	Maternal	2017/ 2017	Moderate	No	None	Medications started
	Fever	Maternal	2017/ 2017	Mild	No	Pregnancy	Medications started
	Laceration, bilateral labial	Maternal	2017/ 2017	Moderate	No	Pregnancy	Other: suture repair
	Laceration, perineal	Maternal	2017/ 2017	Moderate	No	Pregnancy	Other: suture repair
	tachycardia	Maternal	2017/ 2017	Moderate	No	Pregnancy	None
PPD	Vomiting	Maternal	2020/ 2020	Mild	No	Pregnancy	Medications started
	bilateral lower leg edema	Maternal	2020/ 2020	Mild	No	Pregnancy	None

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Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Later First Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	False labor	Maternal	PPD 2020/ 2020	Mild	No	Pregnancy	None
	Cholestasis	Maternal	2020/ 2020	Moderate	No	Pregnancy	Other: Cesarean delivery
	Premature labor result in infant Resp distress	Maternal	2021/ 2021	Moderate	No	Underlying disease	Other: Mother has pre eclampsia history of HTN. She received medication for preeclampsia and c-section performed.

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Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Second Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Bleeding placenta previa-preterm birth	Maternal	PPD 2019/ 2019	Mild	No	Pregnancy	Other: C/S at 36 weeks
	Transfusion	Maternal	2016/ 2016	Mild	No	Pregnancy	Other: transfused 2 U PRBCs prior to scheduled C/S due to anemia
	post partum endometritis	Maternal	2015/ 2015	Mild	No	Pregnancy	Other: Antibiotics
	Preterm labor	Maternal	2018/ 2018	Moderate	Unknown	None	None
	Physical Abuse	Maternal	2017/	Unknown	No	Unknown	None

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Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Second Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	headache	Maternal	PPD 2020/ 2020	Mild	Yes	Underlying disease	Other: changed from Tivicay/Descovy to Biktarvy. Patient exposed to Tivicay/Descovy from PPD 2020 till 2020
	elective termination	Maternal	2020/ 2020	Unknown	No	Other: Patient with unwanted pregnancy, elective	Other: elective abortion
	Rash	Maternal	2018/ 2018	Mild	No	Pregnancy	Medications started
	nausea	Maternal	2015/ 2016	Mild	Yes	Pregnancy	Medications started
	Pelvic pain	Maternal	2015/ 2015	Moderate	No	Pregnancy	Medications started
	sub-chorionic hemorrhage of placenta	Maternal	2018/ 2019	Mild	No	Pregnancy	None

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Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Second Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Snoring	Maternal	PPD 2020/ 2020	Unknown	No	Unknown	None
	Depression	Maternal	2020/ 2020	Unknown	Unknown	Other: History of PTSD, depression, & anxiety	None
	Headache	Maternal	2018/ 2018	Mild	Unknown	Pregnancy	Medications started
	Anemia	Maternal	2018/	Mild	Unknown	Pregnancy	Medications started
	COVID-19	Maternal	2020/ 2020	Mild	No	Unknown	None
	Vomiting	Maternal	2019/ 2020	Mild	No	Pregnancy	Medications started
	Headache	Maternal	2020/ 2020	Moderate	No	Unknown	None
	Bacterial vaginosis	Maternal	2020/ 2020	Moderate	No	Unknown	Medications started
	Appendicitis	Maternal	2020/ 2020	Moderate	No	None	Other: Surgery, appendectomy

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Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Third Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Human Papillomavirus Infection	Maternal	PPD 2017/ 2019	Moderate	No	Unknown	Other: LLETZ procedure, condyloma excision and fulgaration
	condyloma	Maternal	2019/ 2019	Moderate	No	Other: HPV	Other: condyloma excision and fulgaration
	High grade Cervial Intraepithelial neoplasia 2	Maternal	2019/ 2019	Moderate	No	Other: HPV	Other: LLETZ procedure
	Influenza B, systemic inflammatory response syndrome	Maternal	2020/ 2020	Severe	No	Unknown	Medications started
	Pneumonia	Maternal	2020/ 2020	Severe	No	Unknown	Medications started
PPD	proteinuria	Maternal	2017/	Mild	No	Pregnancy	None
	gestational HTN	Maternal	2017/ 2017	Mild	No	Pregnancy	None

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Listing 16.2.7.1
Maternal Adverse Events
(Primary Analysis Population)

Trimester = Third Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Preeclampsia	Maternal	PPD 2016/ 2016	Mild	No	Other: At delivery	Medications started
	nausea/vomiting	Maternal	2013/ 2013	Moderate	No	Concomitant medications	Other: kaletra D/C

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Listing 16.2.7.2
Maternal DTG-related Adverse Events
(Primary Analysis Population)

Trimester = Periconception

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Preterm premature rupture of membrane	Maternal	PPD 2017/ 2017	Unknown	Unknown	Other: Incompetent cervix	Medications started
	post-partum hemorrhage	Maternal	2018/ 2018	Unknown	Unknown	Pregnancy	Other: post-partum blood transfusion
	vomitting	Maternal	2015/ 2016	Mild	Yes	Concomitant medications	Medications started
	nausea	Maternal	2020/	Mild	Yes	Pregnancy	Medications started
	Dizziness, giddiness, and palpitations	Maternal	2020/ 2020	Unknown	Unknown	Unknown	Other: Unknown. Was at different hospital ED department
	Anemia	Maternal	2020/	Unknown	Unknown	Unknown	Other: Unknown. Was at different hospital ED department
	headache	Maternal	2018/ 2018	Moderate	Unknown	Other: Was also complaining of blurry vision and	None

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Note: Adverse events are considered as DTG related if the event is reported as "Yes", "Unknown" or missing.

Listing 16.2.7.2
Maternal DTG-related Adverse Events
(Primary Analysis Population)

Trimester = Periconception

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Vaginal Infection	Maternal	PPD 2017/ 2017	Moderate	Unknown	Unknown	Medications started
	thrombocytopenia	Maternal	2019/	Mild	Unknown	Pregnancy	None

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Note: Adverse events are considered as DTG related if the event is reported as "Yes", "Unknown" or missing.

Listing 16.2.7.2
Maternal DTG-related Adverse Events
(Primary Analysis Population)

Trimester = Second Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Preterm labor	Maternal	PPD 2018/ 2018	Moderate	Unknown	None	None
	headache	Maternal	2020/ 2020	Mild	Yes	Underlying disease	Other: changed from Tivicay/Descovy to Biktarvy. Patient exposed to Tivicay/Descovy from PPD 2020 till 2020
	nausea	Maternal	2015/ 2016	Mild	Yes	Pregnancy	Medications started
	Depression	Maternal	2020/ 2020	Unknown	Unknown	Other: History of PTSD, depression, & anxiety	None
	Headache	Maternal	2018/ 2018	Mild	Unknown	Pregnancy	Medications started
	Anemia	Maternal	2018/	Mild	Unknown	Pregnancy	Medications started

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Note: Adverse events are considered as DTG related if the event is reported as "Yes", "Unknown" or missing.

Listing 16.2.7.3
Infant Adverse Events
(Primary Analysis Population)

Trimester = Periconception

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Autism Spectrum Disorder Requiring Substantial Support (Level 2)	Infant	PPD 2020/	Moderate	Unknown	None	Other: Cognitive and behavioral therapy
	Autism Spectrum Disorder	Infant	2019/	Unknown	Unknown	None	Other: Behavioral therapy and speech therapy
	Missed abortion	Infant	2017/ 2017	Severe	Unknown	Unknown	Other: unknown
	Abortion, Spontaneous	Infant	2018/ 2018	Severe	Unknown	Unknown	None
	Intrauterine fetal death	Infant	2018/ 2018	Severe	Unknown	Unknown	None
	Transient tachypnea	Infant	2017/ 2017	Mild	Unknown	Unknown	None
	Hearing Loss	Infant	2021/	Mild	Unknown	Other: Prematurity	Other: Referral to Specialists: Audiology and also ENT.

[1] W=White, B=Black or African American, A=Asian, I=American Indian or Alaska Native, P=Native Hawaiian or Other Pacific Islander, O=Other.

Listing 16.2.7.3
Infant Adverse Events
(Primary Analysis Population)

Trimester = Later First Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Preterm birth	Infant	PPD 2020/ 2020	Moderate	No	Pregnancy	None
	NICU admission	Infant	2020/ 2020	Mild	No	Other: Neonate required additional respiratory su	Other: CPAP, oxygen, d/c from NICU in <24hr, home with mom at DOL 3
	Autism Spectrum Disorder	Infant	2020/	Moderate	Unknown	None	Other: Behavioral therapy, speech therapy
	Intrauterine growth restriction	Infant	2016/ 2016	Unknown	Unknown	Pregnancy	Other: Admission to NICU for low-birth weight
	positive phencyclidine	Infant	2020/ 2020	Unknown	No	Other: maternal substance abuse	None

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Listing 16.2.7.3
Infant Adverse Events
(Primary Analysis Population)

Trimester = Later First Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Intrauterine fetal demise	Infant	PPD 2019/ 2019	Unknown	Unknown	Unknown	Other: This was a patient who had multiple co-morbidities as listed in the platform. She was non adherent to care. Since this is a retrospective chart review we only have and can report the information documented and recorded in the EMR. There is no note by the physician that discusses possible causes of death. As documented this was a 28 week fetal demise with pleural effusion diagnosed on ultrasound. This is in the report we submitted. That is what is documented. The study drug information is listed in the data base. There is a pathology report that describes findings (subchorionic hematoma and placenta infarct) but does not report causality.

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Listing 16.2.7.3
Infant Adverse Events
(Primary Analysis Population)

Trimester = Later First Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Hydrops Fetalis	Infant	PPD 020/ 020	Severe	Unknown	Unknown	None
	fetal Anemia	Infant	020/ 020	Severe	Unknown	Unknown	None
	Infant Resp distress	Infant	021/ 021	Moderate	No	Other: Mother underlying disease: pre eclampsia h	Other: Infant on room air for first 24 hrs, then intubated on day 2 and by day 3 extubated, provided IV fluids and caffeine bolus. Room air day 3 remained in NICU until discharged at 35 2/7 GA on PPD /21. Birth and 14 day HIV PCR neg.

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Listing 16.2.7.3
Infant Adverse Events
(Primary Analysis Population)

Trimester = Later First Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Supraventricular tachycardia	Infant	PPD 021/ 021	Mild	Unknown	Unknown	Other: Reverted to Sinus Rhythm after placing cold water on the head . EKG was normal and Echo ordered PPD /2021. Echo: 1. Left-sided patent ductus arteriosus. Very small. Shunt flow is left to right and throughout the cardiac cycle. 2. Atrial septum: There is a small patent foramen ovale. There is a small left-to-right shunt through a patent foramen ovale. 3. Normal left ventricle systolic function. 4. Normal coronary arteries. Mother reports she attended a follow up peds cardiology 2 weeks following discharge (baby 2 weeks old) and informed everything was fine and no need for further visits.

[1] W=White, B=Black or African American, A=Asian, I=American Indian or Alaska Native, P=Native Hawaiian or Other Pacific Islander, O=Other.

Listing 16.2.7.3
Infant Adverse Events
(Primary Analysis Population)

Trimester = Second Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Stillbirth	Infant	PPD 2020/ 2020	Severe	Unknown	Unknown	Other: vaginal delivery
	intrauterine fetal demise, stillbirth	Infant	2015/ 2015	Severe	No	Underlying disease	Other: induction of labor
	Intrauterine fetal death	Infant	2017/ 2017	Severe	Unknown	Unknown	None

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Listing 16.2.7.3
Infant Adverse Events
(Primary Analysis Population)

Trimester = Third Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	SIDS	Infant	PPD 2018/ 2018	Severe	No	Other: SIDS	None
	umbilical hernia	Infant	2017/ 2017	Mild	No	None	None

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Listing 16.2.7.4
Infant DTG-related Adverse Events
(Primary Analysis Population)

Trimester = Periconception

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Autism Spectrum Disorder Requiring Substantial Support (Level 2)	Infant	PPD 020/	Moderate	Unknown	None	Other: Cognitive and behavioral therapy
	Autism Spectrum Disorder	Infant	019/	Unknown	Unknown	None	Other: Behavioral therapy and speech therapy
	Missed abortion	Infant	017/ 017	Severe	Unknown	Unknown	Other: unknown
	Abortion, Spontaneous	Infant	018/ 018	Severe	Unknown	Unknown	None
	Intrauterine fetal death	Infant	018/ 018	Severe	Unknown	Unknown	None
	Transient tachypnea	Infant	017/ 017	Mild	Unknown	Unknown	None
	Hearing Loss	Infant	021/	Mild	Unknown	Other: Prematurity	Other: Referral to Specialists: Audiology and also ENT.

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Note: Adverse events are considered as DTG related if the event is reported as "Yes", "Unknown" or missing.

Listing 16.2.7.4
Infant DTG-related Adverse Events
(Primary Analysis Population)

Trimester = Later First Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Autism Spectrum Disorder	Infant	PPD 2020/	Moderate	Unknown	None	Other: Behavioral therapy, speech therapy
	Intrauterine growth restriction	Infant	2016/ 2016	Unknown	Unknown	Pregnancy	Other: Admission to NICU for low-birth weight

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Note: Adverse events are considered as DTG related if the event is reported as "Yes", "Unknown" or missing.

Listing 16.2.7.4
Infant DTG-related Adverse Events
(Primary Analysis Population)

Trimester = Later First Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Intrauterine fetal demise	Infant	PPD 2019/ 2019	Unknown	Unknown	Unknown	Other: This was a patient who had multiple co-morbidities as listed in the platform. She was non adherent to care. Since this is a retrospective chart review we only have and can report the information documented and recorded in the EMR. There is no note by the physician that discusses possible causes of death. As documented this was a 28 week fetal demise with pleural effusion diagnosed on ultrasound. This is in the report we submitted. That is what is documented. The study drug information is listed in the data base. There is a pathology report that describes findings (subchorionic hematoma and placenta infarct) but does not report causality.

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Note: Adverse events are considered as DTG related if the event is reported as "Yes", "Unknown" or missing.

Listing 16.2.7.4
Infant DTG-related Adverse Events
(Primary Analysis Population)

Trimester = Later First Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Hydrops Fetalis	Infant	PPD 2020/ 2020	Severe	Unknown	Unknown	None
	fetal Anemia	Infant	2020/ 2020	Severe	Unknown	Unknown	None

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Note: Adverse events are considered as DTG related if the event is reported as "Yes", "Unknown" or missing.

Listing 16.2.7.4
Infant DTG-related Adverse Events
(Primary Analysis Population)

Trimester = Later First Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Supraventricular tachycardia	Infant	PPD 021/ 021	Mild	Unknown	Unknown	Other: Reverted to Sinus Rhythm after placing cold water on the head . EKG was normal and Echo ordered PPD 2021. Echo: 1. Left-sided patent ductus arteriosus. Very small. Shunt flow is left to right and throughout the cardiac cycle. 2. Atrial septum: There is a small patent foramen ovale. There is a small left-to-right shunt through a patent foramen ovale. 3. Normal left ventricle systolic function. 4. Normal coronary arteries. Mother reports she attended a follow up peds cardiology 2 weeks following discharge (baby 2 weeks old) and informed everything was fine and no need for further visits.

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Note: Adverse events are considered as DTG related if the event is reported as "Yes", "Unknown" or missing.

Listing 16.2.7.4
Infant DTG-related Adverse Events
(Primary Analysis Population)

Trimester = Second Trimester

Subject ID/ Age/Race[1]	Event Name	Type of Event	Onset Date/ Resolution Date	Severity	Relationship to DTG	Other suspected cause; Specify	Treatment Event; Specify
PPD	Stillbirth	Infant	PPD 2020/ 2020	Severe	Unknown	Unknown	Other: vaginal delivery
	Intrauterine fetal death	Infant	2017/ 2017	Severe	Unknown	Unknown	None

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Note: Adverse events are considered as DTG related if the event is reported as "Yes", "Unknown" or missing.