Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)

Title	:	Reporting and Analysis Plan for ING200336: A Prospective, Interventional Pharmacokinetic and Safety Study of DTG/ABC/3TC in Pregnant Women
Compound Number	:	GSK1349572+GR109714+GI265235 (GSK2619619)
Clinical Study Identifier	:	ING200336
Effective Date	:	03-MAR-2021

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 200336.
- This RAP is intended to describe all the planned analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverables.

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for Protocol: 200336

Revision Chronology:		
GlaxoSmithKline Document Number	**Date**	**Version**
2013N166290_00	18-DEC-2013	Original
2013N166290_01	15-APR-2014	Amendment No.: 01
2013N166290_02	23-APR-2014	Amendment No.: 02
2013N166290_03	19-JUN-2018	Amendment No.: 03

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Changes from the originally planned statistical analysis specified in the protocol are outlined in Table 1.

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	**Reporting & Analysis Plan**	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• **Pharmacokinetic Analysis**: • Log-transformed PK parameters except tmax will be analysed by analysis of variance	• No ANOVA will be done.	• Very few subjects will be recruited

• **Efficacy Endpoints for Infants:**
  • Proportion of subjects with plasma HIV-1 RNA < 50 c/mL and <400 c/mL over time.
  • Absolute values and changes from Baseline in CD4+ T cell counts over time.
  • Incidence of disease progression (HIV-associated conditions, acquired immunodeficiency syndrome [AIDS] and death).
	• These data were not collected for Infants.	• Inconsistencies within the protocol. The data for these endpoints were not collected in infants.

2.2. Study Objectives and Endpoints

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
Mother	
• To describe the total plasma DTG PK parameters with the DTG/ABC/3TC FDC during Weeks 18-26, Weeks 30 – 36 of the third trimester of the pregnancy and 8-12 weeks postpartum	• Area under the concentration-time curve during a 24-hour interval at steady state [AUC24], maximal drug concentration [Cmax], drug concentration at the end of dosing interval [Cτ], Tmax, C0, apparent clearance [CL/F[, steady state volume of distribution [Vss/F] and the half-life [t½]) of DTG
• To further characterize the safety and tolerability of DTG/ABC/3TC FDC when used during pregnancy	• Incidence and severity of AEs and laboratory abnormalities. • Absolute values and changes over time in laboratory parameters; • Proportion of subjects who discontinue treatment due to AEs;
Secondary Objectives	**Secondary Endpoints**
Mother	
• To assess the antiviral activity of the DTG/ABC/3TC FDC when administered during pregnancy	• Absolute values and change from Baseline HIV1 RNA over time. • Proportion of subjects with plasma HIV-1 RNA <50 and <400 c/mL over time
• To assess the immunologic activity of DTG/ABC/3TC FDC	• Absolute values and change from Baseline in CD4+ cell count over time.
• Incidence of disease progression	• HIV-associated conditions, acquired immunodeficiency syndrome [AIDS] and death
• To assess the incidence of treatment – emergent genotypic and phenotypic resistance in subjects who meet virologic withdrawal criteria	• Treatment-emergent genotypic and phenotypic resistance in subjects who meet confirmed virologic withdrawal criteria
• To evaluate the unbound DTG concentrations in plasma during Weeks 18-26 and Weeks 30-36 of the pregnancy and 8-12 weeks postpartum	• Unbound concentrations and Unbound fraction at 3 and 24 hours post dose in the third trimester and postpartum.
• To compare the DTG concentrations in plasma from cord blood with those in maternal plasma at the time of delivery	• Total DTG concentrations in plasma from cord blood and those in maternal plasma at the time of delivery.
• To characterize pregnancy (maternal) outcomes	• Pregnancy outcomes; Pregnancy risks

Objectives	Endpoints
• To characterize birth outcomes	• Birth outcomes (per pregnancy outcomes endpoint above)
Infant	
• To characterize infant outcomes at birth	• Infant outcomes at birth
• To characterize the safety of DTG/ABC/3TC FDC to the developing fetus	• Proportion of pregnancies with and without demonstrated congenital malformations

2.3. Study Design

Overview of Study Design and Key Features	
Design Features	• This is a single arm open-label interventional study for women who become pregnant while participating in ING117172 on the DTG/ABC/3TC FDC treatment arm.
Dosing	• All subjects will be administered DTG 50 mg/ABC 600 mg/3TC 300 mg FDC tablet administered once daily.
Time & Events	• [Refer to Appendix 1: Schedule of Activities]
Treatment Assignment	• Subjects will initiate therapy with DTG/ABC/3TC FDC following confirmation of fulfilment of study entry criteria. A unique treatment number will be assigned for each subject participating in the study. Subjects who are enrolled into the trial and subsequently withdrawn may not be re-screened.
Interim Analysis	• No interim analysis was planned, however protocol allowed further data cuts and analyses to be conducted as necessary to support regulatory requests, submissions and/or publications. The study recruitment was terminated early which triggered reporting of the primary endpoint.

2.4. Statistical Hypotheses / Statistical Analyses

This is a single arm open-label interventional study for women who become pregnant while participating in ING117172. No formal hypotheses testing will be performed.

2.5. Interim Analyses

No interim analyses were formally planned, however the protocol allows further data cuts and analyses are conducted as necessary to support regulatory requests, submissions and/or publications. The planned analyses will be performed after the completion of the following sequential steps:

1. Subjects are considered to have completed the study after completing the postpartum evaluation approximately 8-12 weeks post-delivery. The primary outcome analyses will take place after the last subject enrolled gives birth and completes their last visit.

2. All required database cleaning activities have been completed.

2.6. Final Analyses

Subjects may continue to receive DTG/ABC/3TC FDC after completion of the primary endpoint assessments, until study medications are locally approved and commercially available (or they meet a criteria for withdrawal). During this time, subjects will be monitored every 12 weeks to ensure they continue to derive clinical benefit from DTG/ABC/3TC FDC.

A final End-of-Study analysis will be conducted when all subjects have completed the study and final database release (DBR), source data lock (SDL) and database freeze (DBF) have been declared by Data Management.

3. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All subjects Screened	• All participants who were screened for eligibility	• Study Population
Enrolled	• All participants who passed screening and entered the study	• Study Population
Safety/ITT-E	• All participants who received at least one dose of study treatment.	• Study Population • Safety • Efficacy
Pharmacokinetic (PK)	• All participants in the Safety population who had at least 1 non-missing PK assessment (Non-quantifiable [NQ] values will be considered as missing values) • Note: PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded.	• PK

Refer to Appendix 9: List of Data Displays which details the population used for each display.

3.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) and non-important COVID-19 related protocol deviations will be listed.

4. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

4.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
Data Displays for Reporting			
Code	Description	Description	Order
A	DTG/ABC/3TC FDC once daily	DTG/ABC/3TC	1

No subgroup analysis will be done.

4.2. Baseline Definitions

For all endpoints (unless otherwise stated) the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

Unless otherwise stated, if baseline data are missing no derivation will be performed and baseline will be set to missing.

Unless otherwise specified, the baseline definitions specified in the table below will be used for derivations for endpoints/parameters and indicated on listings.

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit Value – Baseline
% Change from Baseline	= 100 x [(Post-Dose Visit Value – Baseline) / Baseline]

4.3. Multicentre Studies

There are no planned adjustments made for multiple centres in this study.

4.4. Examination of Covariates, Other Strata and Subgroups

No covariates, Strata or Subgroups will be considered for descriptive summaries or Statistical analysis.

4.5. Other Considerations for Data Analyses and Data Handling Conventions

Other considerations for data analyses and data handling conventions are outlined in the appendices:

Section	Component
11.2	Appendix 2 : Assessment Windows
11.3	Appendix 3: Study Phases and Treatment Emergent Adverse Events
11.4	Appendix 4: Data Display Standards & Handling Conventions
11.5	Appendix 5: Derived and Transformed Data
11.6	Appendix 6: Reporting Standards for Missing Data
11.7	Appendix 7: Values of Potential Clinical Importance

5. STUDY POPULATION ANALYSES

5.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the Enrolled and ITT-E population.

Table 2 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 9: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Display Type	Data Display's Generated	
	Table	Listing
Randomisation		
Randomisation		Y
Subject Disposition		
Study Populations		Y
Subject Recruitment by country and site ID	Y	Y
Disposition (overall and by relationship to COVID-19 Pandemic)	Y	
Reasons for Withdrawal		Y
Study Visit Dates		Y
Protocol Deviations		
Important Protocol Deviations		Y
Non-Important COVID-19 related Protocol Deviations		Y
Demography and Baseline Characteristics		
Demographic Characteristics	Y	Y
Age Ranges	Y	
Race	Y	Y
CDC Classification of HIV infection at Baseline		Y
Cardiovascular Risk Assessments at Baseline		Y
History of Cardiac Therapeutic Procedures		Y
Cardiovascular Events at Baseline		Y
Maternal History (Pregnancy History)		Y
Medical Conditions, Concomitant Medications & Antiretroviral Therapy		
Medical Conditions (Current and Past)		Y
Concomitant Medications (non-ART)		Y [1]
Prior and Concomitant ART Medications		Y [2]

Display Type	Data Display's Generated	
	Table	Listing
Other		
Investigational Product		Y

Notes:

- Y = Display Generated

1. One listing for concomitant non-ART medications and one listing showing the relationship between verbatim text, ingredient and ATC Level 1.
2. One listing for Prior ART, one listing for concomitant ART and one listing showing the relationship between verbatim text, ingredient, combination and ATC Level 4.

6. EFFICACY ANALYSES

6.1. Endpoint / Variables

Mother

- Absolute value and change from baseline in HIV-1 RNA over time
- Proportion of subjects with plasma HIV-1 RNA <50 and <400 c/mL over time
- Absolute value and change from baseline in CD4+ Cell count over time
- Disease progression and HIV associated conditions

6.2. Summary Measure

Efficacy data will be presented in tabular form and will be summarized descriptively by visit.

6.3. Population of Interest

The efficacy analyses will be based on the Intent-To-Treat- Exposed population, unless otherwise specified.

6.4. Strategy for Intercurrent (Post-Randomization) Events

Not applicable.

6.5. Efficacy Analyses / Methods

Details of the planned displays are provided in Appendix 9: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 6.1 will be listed and summarised.

Table 3 Overview of Planned Efficacy Analyses

Endpoints	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Quantitative Plasma HIV-1 RNA								
Observed over time				Y	Y			
Proportion of Subjects with Plasma HIV-1 RNA <400 copies/mL	Y							
Proportion of Subjects with Plasma	Y							

Endpoints	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
HIV-1 RNA <50 copies/mL								
CD4+ Cell Count								
Observed over time				Y	Y			
Post-baseline HIV-1 Disease Progression								
Incidence of disease progression[1]	Y							

NOTES: L = Listing, Y = Yes display generated.

1. HIV-associated conditions, acquired immunodeficiency syndrome [AIDS] and death

7. SAFETY ANALYSES

The safety analyses will be based on the Safety population, unless otherwise specified.

7.1. Adverse Events Analyses

The details of the planned displays are provided in Appendix 9: List of Data Displays.

Table 4 Overview of Planned Safety Analyses

Display Type	Absolute	
	Summary	Individual
	T	L
Exposure Data		Y
All Adverse Events		Y
Non-Fatal serious Adverse Events		Y
Non-Serious Drug-Related Adverse Events by Overall Frequency	Y	
All Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity	Y	
Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	Y	
Grade 2-4 Adverse Events by Overall Frequency	Y	
Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	Y	
Serious Fatal and Non-Fatal Drug-Related Adverse Events by Overall Frequency	Y	

Display Type	Absolute	
	Summary	Individual
	T	L
Reasons for Considering as a Serious Adverse Event		Y
Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study	Y	Y
Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		Y
COVID-19 Assessments and Symptom assessments		Y

NOTES: • T = Table, L = Listing, Y = Yes display generated.

7.2. Clinical Laboratory and Other Safety Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Haematology laboratory tests and Urinalysis, and non-laboratory safety test results including vital signs, cardiovascular events and suicidality monitoring tests will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 9: List of Data Displays.

Endpoint	Absolute				Change from Baseline					Max Post BL		
	Summary		Individual		Stats Analysis			Summary		Summary		
	T	F	F	L	T	F	L	T	F	T	F	L
Laboratory values												
Clinical Chemistry				Y				Y		Y		
Haematology				Y				Y		Y		
Urinalysis				Y				Y				
Non-Laboratory values												
Vital Signs				Y								
Suicidal Ideation and Behaviour Data				Y								
Others												
COVID-19 Symptom and assessments				Y								

NOTES: T=Table, F=Figure, L = Listing, Y = Yes display generated

8. PHARMACOKINETIC ANALYSES

8.1. Primary and Secondary Pharmacokinetic Analyses

8.1.1. Endpoint / Variables

Pharmacokinetic parameters will be determined from the plasma concentration-time data, as data permits.

Primary PK Analysis Endpoints:

DTG AUC(0-τ), Cmax, Cτ, CL/F, Vss/F, and $t_{1/2}$ based on intensive PK sampling during the second and third trimesters of pregnancy (Weeks 18-26 and 30-36) and at 8-12 weeks postpartum will be determined, as data permits.

Secondary PK Analysis Endpoints

- C0 and Tmax based on intensive PK sampling during the second and third trimesters of pregnancy (Weeks 18-26 and 30-36) and at 8-12 weeks postpartum
- C3h,u and C24h,u and fu at the PK visits during the second and third trimesters and at 8-12 weeks postpartum
- Total DTG concentrations in plasma from cord blood compared to those in maternal plasma at the time of delivery.

8.1.1.1. Drug Concentration Measures

All PK concentration summary and listing displays will be based on Pharmacokinetic population. Concentrations of DTG in plasma will be listed and summarized according to GSK standards, where applicable (Refer to Appendix 4: Data Display Standards & Handling Conventions (Section 11.4.3 Reporting Standards for Pharmacokinetic).

DTG concentration listings for the PK population will be sorted by subject and time relative to dose, noting the study visit; summaries will be presented by time relative to dose at each PK visit -Weeks 18-26 and Weeks 30-36 of pregnancy, and at 8-12 weeks post-partum (See Appendix 2: Section 11.2.3 for details) . At each PK visit, samples will be collected prior to dosing and at 1,2, 3, 4, 6, 8, 12 and 24 hours post dosing. The pre-dose sample should be collected within 15 minutes prior to the dose on the day of PK visit. DTG concentrations in plasma from cord blood will also be collected at the time of delivery will be compared with those in maternal plasma at the time of delivery.

8.1.1.2. Derived Pharmacokinetic Parameters

PK analysis will be the responsibility of the Clinical PK Modeling & Simulation department within GlaxoSmithKline. Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin 5.2 or higher. All calculations of non-

compartmental parameters will be based on actual sampling times recorded during the study. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data, as data permits.

Table 5 Table of Derived PK Parameters

Parameter	Parameter Description
AUC(0-τ)	DTG Area under the plasma concentration time curve at steady state during a dosing interval
C0	DTG Pre-dose plasma concentration
Cmax	DTG maximum observed plasma concentration determined directly from the concentration-time data.
Tmax	Time to reach Cmax, determined directly from the concentration-time data.
Cτ	Drug concentration at the end of dosing interval.
CL/F	Apparent oral clearance.
Vss/F	Apparent volume of distribution after extravascular (e.g., oral) administration.
t½	DTG half-life.
C3h,u	Unbound DTG concentration in plasma at 3 hours post dose
C24h, u	Unbound DTG concentration in plasma 24 hours post dose
Weight Normalised CL/F	Apparent oral clearance
Weight Normalised Vss/F	Apparent volume of distribution after extravascular (e.g., oral) administration
fu3h and fu24h	Unbound fraction at 3 hours and 24 hours post dose, calculated as: fu = Cunbound/Ctotal where Cunbound and Ctotal are the unbound and total concentration of DTG in plasma, respectively.

8.1.2. Summary Measure

Pharmacokinetic data will be presented in graphical and/or tabular form and will be summarized descriptively by time relative to dose at each PK visit -Weeks 18-26 and Weeks 30-36 of pregnancy, and at 8-12 weeks post-partum (See Appendix 2: Section 11.2.3 for details) .

8.1.3. Population of Interest

The primary pharmacokinetic analyses will be based on the Pharmacokinetic population, unless otherwise specified.

8.1.4. Strategy for Intercurrent (Post-Randomization) Events

Not Applicable.

8.1.5. Statistical Analyses / Methods

Unless otherwise specified, endpoints / variables defined in Section 8.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

Table 6 provides an overview of the planned analyses, with full details being presented in Appendix 9: List of Data Displays.

Table 6 Overview of Planned Pharmacokinetic Analyses

End Point	Untransformed				Log-Transformed			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
PK Concentrations								
Plasma DTG Concentrations	Y	Y	Y	Y	Y	Y	Y	
PK Parameters								
Plasma DTG Parameters	Y			Y	Y			

Note: T= Table, F=Figure, L=Listing, Y = Yes display generated

9. MATERNAL AND INFANT ANALYSES

9.1. Maternal Outcomes

9.1.1. Endpoints/Variables

- Pregnancy outcomes variables: Spontaneous loss/miscarriage, Elective termination, Still birth, Live birth. In case of Live birth applicable Birth outcome categories will be listed.
- Maternal History
- Previous and Current Pregnancy risk assessment

9.1.2. Summary Measure

Current Maternal data will be summarised over each maternal outcome.

9.1.3. Population of Interest

The Maternal Outcome analysis will be based on the Safety population, unless otherwise specified.

9.1.4. Strategy for Intercurrent (Post-Randomization) Events

Not applicable.

9.1.5. Statistical Analyses/ Methods

Details of the planned displays are provided in Appendix 9: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, all endpoints / variables defined in Section 9.1.1 will be listed. The pregnancy outcomes will be summarised.

9.2. Infant Outcomes

9.2.1. Endpoints/Variables

Infant outcome variables:

- Infant gestational age,
- Gestational length,
- Gestational weight (including percentiles, SGA, AGA, LGA, IUGR [IUGR in case of SGA only])
- Head circumference
- APGAR (Appearance, Pulse Rate, Grimace Reflex, Activity, Respiration) one and five minute scores
- Presence or absence of major congenital abnormalities at birth.
- HIV Status of Infant at 8-12 week postpartum visit

9.2.2. Summary Measure

The Infant data will be summarised over each outcome.

9.2.3. Population of Interest

The Infant Outcome analysis will be based on the Safety Population, unless otherwise specified.

9.2.4. Strategy for Intercurrent (Post-Randomization) Events

Not applicable.

9.2.5. Statistical Analyses/ Methods

Details of the planned displays are provided in Appendix 9: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 9.2.1 will be listed and summarised.

10. VIROLOGY ANALYSIS

10.1.1. Endpoints/Variables

Treatment-emergent genotypic and phenotypic resistance in subjects who meet confirmed virologic withdrawal criteria

10.1.2. Population of Interest

The virology analyses will be based on the ITT-E population, unless otherwise specified.

10.1.3. Statistical Analyses/Methods

Details of the planned displays are provided in Appendix 9: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoint defined in Section 10.1.1 will be summarised.

11. APPENDICES

11.1. Appendix 1: Schedule of Activities

11.1.1. Protocol Defined Schedule of Events

Procedures	Screen*,**	Day 1	Ante partum	Delivery	Post-Partum	Continuation Phase	Withdrawal	Follow-up[12]
			Monthly – every 4 weeks		8-12 weeks post delivery	Every 12 weeks after Post Partum Visit		
Written Informed Consent	X							
Inclusion/Exclusion Criteria	X	X						
Subject Demography	X							
Medical History[1]		X			X	X		
Concurrent medical conditions		X						
CDC HIV-1 classification		X						
HIV-associated conditions			X	X	X	X	X	X
Cardiovascular risk assessment[2]	*							
Prior Art history	*							
Gravidity Maternal history		X						
Pregnancy risk assessment	X	X	X					
Uteroplacental Outcomes at Delivery[3]				X				
Infant Outcomes[4]				X	X	X		X
Concomitant Medication	X	X	X	X	X	X	X	X
Limited Physical Examination[5]		X	X		X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X

Procedures	Screen*,**	Day 1	Ante partum	Delivery	Post-Partum	Continuation Phase	Withdrawal	Follow-up[12]
			Monthly – every 4 weeks		8-12 weeks post delivery	Every 12 weeks after Post Partum Visit		
Serious Adverse Events[6]	X	X	X	X[5]	X	X	X	X
Pharmacokinetic Sampling[7]			X[6]	X	X			
Cord & maternal blood sample[8]				X				
Columbia Suicidality Severity Rating Scale[9]		X	X		X	X	X	
Laboratory Assessments								
Pregnancy Assessment		X			X	X		
Hematology	**	**	X		X	X	X	X
Clinical Chemistry	**	**	X		X	X	X	X
Urinalysis. Including dipstick for protein analysis	**		X		X	X		X
Quantitative plasma HIV-1 RNA[10]	**	**	X	X	X	X	X	
Lymphocyte subsets	**	**	X	X[5]	X	X		X
PGx Sampling[11]		X						
Plasma for storage[12]	X	X	X	X	X	X	X	X
Dispense IP		X	X	X	X	X[11]		

*Baseline information, including cardiovascular risk and prior ART therapy will be transferred from ING117172 to serve as baseline/screening data in this study.

**HIV-1 RNA, lymphocyte subset, and laboratory assessment (hematology, chemistry, and urinalysis including a dipstick) data collected at the ING117172 unscheduled or last visit within 28 days of learning of the pregnancy will be transferred to serve as screening data in this study. The ING117172 Withdrawal visit will serve as the ING200336 Day 1.

Gravidity: Maternal history and pregnancy risk assessment may occur at either Screening or Day 1 visit.

1. Medical History includes any changes in smoking status
2. Assessment for cardiovascular risk will include height, weight, blood pressure, smoking history, medical conditions and will have previously been collected in ING117172
3. Assessment of pregnancy outcomes (e.g., spontaneous losses, induced abortions, still births, pre-term births, preeclampsia)
4. Assessment of maternal and infant outcomes, including live births, gestational age, presence or absence of major congenital abnormalities, and infant height, weight, [including percentiles, SGA, AGA, LGA, IUGR], head circumference, and presence or absence of major congenital abnormalities at birth. If known, HIV status of the infant will be collected at the 8-12 week post-partum visit.
5. Limited physical examination to include blood pressure at Baseline (recorded in eCRF), heart rate and weight at each visit (recorded in eCRF at Baseline and on lab requisition at all visits) for determination of CrCL. Blood pressure to be measured after resting in a semi-supine position for at least 5 minutes.
6. From the time a subject consents to participate in ING200336 and administration of IP at Day 1, only SAEs assessed as related to study participation (e.g., study treatment, protocol-mandated procedures, invasive tests, or change in existing therapy) or related to a GSK concomitant medication, will be recorded in the eCRF for ING200336. Only SAEs related to study participation or to a concomitantly administered GSK or ViiV product will be collected between obtaining informed consent and administration of IP at Day 1.

Note: At the time of the Withdrawal visit in ING117172 if there is an ongoing, unresolved adverse event (AE) and/or serious adverse event (SAE) it will be left in ING117172 as

unresolved and transcribed as medical history in ING200336. If the AE and/or SAE worsen after enrollment into ING200336 it will be recorded on the AE/SAE forms in ING200336.
7. Intensive PK visit: The PK evaluations should be scheduled for study visits at Weeks 18-26, Weeks 30-36 and 8-12 weeks postpartum. The DTG dose on serial PK sampling days is to be given with a light meal/snack PK should be scheduled so that witnessed dosing of DTG/ABC/3TC FDC is as close as possible to 24 hours (generally 22-26 hours) after the previous dosing. The PK visit should be re-scheduled if the subject took their morning dose prior to coming into the clinic on the PK sampling day. See SPM for additional details.
8. If feasible, a cord and maternal blood sample will also be collected at delivery and if possible within 30 minutes of each other.
9. Suicidality Questionnaire will be conducted q 12 weeks during the Continuation Phase.
10. HIV-1 RNA and lymphocyte to be drawn within 24 hours of delivery and on the day of the post-partum PK evaluation.
11. The PGx sample should be collected at Day 1 if not collected during participation in ING117172, however this sample may be collected at any time during the study.
12. Plasma samples for storage will be collected at each visit for possible future analyses (including but not limited to HIV-1 RNA genotypic and phenotypic analyses in confirmed cases of subject withdrawal, HIV-1 RNA levels, when samples are lost or arrive at the laboratory unevaluable, and immunological parameters.)
13. Only for subjects who continue DTG/ABC/3TC and are seen in the clinic every 12 weeks until DTG/ABC/3TC is commercially available locally. Note: after delivery, subjects must use one of the contraception methods to avoid a ‘new’ pregnancy
14. A Follow up visit may be conducted approximately 4 weeks after the last dose of study provided IP, and is required only if the subject has ongoing SAEs or non-serious AEs (as outlined in the SPM) at the last on study visit. The assessments performed should reflect what is considered medically necessary to assess the event(s).

11.2. Appendix 2: Assessment Windows

Laboratory data and vital signs will be assigned to assessment windows according to actual dates rather than the nominal visit labels as recorded on the eCRF or in the laboratory database.

A window around a target Study Day will typically include all days from the midpoints between it and the target Study Days of the previous and the proceeding visits. In general, the nominal target study day for week w is (7*w)+1.

11.2.1. Definitions of Assessment Windows for Analyses

Analysis Set / Domain	Parameter (if applicable)	Target	Analysis Window		Analysis Timepoint
			Beginning Timepoint	Ending Timepoint	
All	All				Screening
		1			Day 1
		29	2	42	Week 4
		57	43	70	Week 8
		85	71	98	Week 12
		113	99	126	Week 16
		141	127	154	Week 20
		169	155	182	Week 24
		197	183	210	Week 28
		225	211	238	Week 32
		253	239	266	Week 36
		281	267	294	Week 40
		337	295	378	Week 48
		7*w+1	7*w-41	7*w+42	Week w, w=52, 64, 76, ...
		Study Day of last dose + 28	>Study Day of last dose +1	>Study Day of last dose +1	Follow-up

NOTES:

- For parameters which are not scheduled to be assessed at particular visits, the all-inclusive windows defined will still be used.
- Assessments at unscheduled visits will be included for 'any time On-treatment' time points and in data listings.

11.2.2. Definitions of Assessment Windows for Inclusion in the PK Analysis

The windows for inclusion of PK samples in summary statistics for all PK visits will be as follows:

- Samples collected 15 minutes prior to dose for pre-dose sample
- Samples collected within ±15 min of the 1h and 2h time points
- Samples collected within ± 30 min of the 3h, 4h, 6h time points
- Samples collected within ± 1h for the 8h and 12h time points
- Samples collected within ± 2h for the 24 h time point

11.2.3. Stages of Pregnancy used for Pharmacokinetics

Stage		Weeks
Ante-Partum	Trimester 2	18-26
	Trimester 3	30-36
Delivery		
Post-Partum		

NOTES:

- Delivery is a single day.
- Post-partum PK assessment is done 8-12 weeks after delivery

11.2.4. Analysis visits in relation to pregnancy

In addition, an analysis visit in relation to pregnancy is derived, which will also be listed in the listings.

- For the screening, delivery and post-partum visits, the same scheduled visit is used.
- For the Day 1 and ante-partum visits, the corresponding gestation weeks from reproductive system findings is used.
- For the subsequent post-partum visits, the analysis visit in relation to pregnancy is derived by (visit day of subsequent post-partum visit - visit day at post-partum)/7.

11.3. Appendix 3: Study Phases and Treatment Emergent Adverse Events

11.3.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to Study Visits.

11.3.1.1. Treatment States for Laboratory, HIV Associated Conditions, Vital Signs, and Genotypic and Phenotypic Data

Study Phase	Definition
Pre-Treatment	Date ≤ Study Treatment Start Date
On-Treatment	Study Treatment Start Date < Date ≤ Study Treatment Stop Date + 1
Post-Treatment	Date > Study Treatment Stop Date + 1

11.3.1.2. Treatment States for Prior/Concomitant/Post-Therapy Medications Data

- Prior medications are those taken (i.e., started) before the start date of investigational product.
- Concomitant medications are those taken (i.e., started or continued) at any time between the start date and stop date of IP, inclusive. Prior medications that were continued during this period are also considered as concomitant medications.
- Post-treatment medications are those started after the stop date of IP. Concomitant medications that were continued during this period are also considered as post-treatment medications.

It will be assumed that medication has been taken on the date in which it is reported as started or stopped. Also, for any medication starting on the same date as IP, it will be assumed that the medication was taken after the subject started taking IP.

ART medications will also be classified as prior, concomitant and/or post-treatment according with the following modifications:

- ART starting on study treatment stop date will be considered as only post-treatment and not concomitant. It is expected that after discontinuation of study treatment, a subject may immediately begin taking another ART.
- ART stopping on study treatment start date will only be considered as prior and not concomitant.
- Any ART entered on the Prior ART eCRF with partial end date will be assumed to have finished before Screening.

	Pre-treatment	On-treatment			Post-treatment		Prior	Conco-mitant	Post
		IP Start Date		IP Stop Date	IP Stop Date+1				
(a)	x————x						Y	N	N
(b)	x————		————x				Y	Y	N
(c)	x————		————			————x	Y	Y	Y
(d)			x————x				N	Y	N
(e)			x————			————x	N	Y	Y
(f)						x————x	N	N	Y
(g)	?————x						Y	N	N
(h)	?————		————x				Y*	Y	N
(i)	?————		————			————x	Y*	Y*	Y
(j)	x————		————			————?	Y	Y**	Y**
(k)			x————			————?	N	Y	Y**
(l)						x————?	N	N	Y
(m)	?————		————			————?	Y***	Y***	Y***
(n)	x————	x					Y	Y	N
(o)	?————	x					Y*	Y	N
(p)		x	————x				N	Y	N
(q)		x	————	x			N	Y	N
(r)				x	—	————x	N	Y	Y
(s)				x	—	————?	N	Y	Y**
(t)					x	————x	N	N	Y
(u)					x	————?	N	N	Y
(v)			x————	—	x		N	Y	Y

x = start/stop date of medication
? = missing start/stop date of medication
* If a medication is stopped On-treatment or Post-treatment and no start date is recorded it will be assumed that the medication was ongoing from the Pre-treatment phase
** If a medication is started Pre-treatment or On-treatment and no stop date is recorded then usage will be assumed to be ongoing for the remainder of the study
*** If a medication has no start or stop date it will be assumed that the medication was ongoing from the Pre-treatment phase to the Post-treatment phase

11.3.1.3. Treatment States for AE Data

Treatment State	Definition
Pre-Treatment	AE Start Date < Study Treatment Start Date
On-Treatment	If AE onset date is on or after treatment start date & on or before treatment stop date. Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date
Post-Treatment	If AE onset date is after the treatment stop date. AE Start Date > Study Treatment Stop Date
Onset Time Since 1st Dose (Days)	If Treatment Start Date > AE Onset Date = AE Onset Date - Treatment Start Date If Treatment Start Date ≤ AE Onset Date = AE Onset Date - Treatment Start Date +1

Treatment State	Definition
	Missing otherwise.
Duration (Days)	AE Resolution Date – AE Onset Date + 1
Drug-related	If relationship is marked 'YES' on CRF.

NOTES:

- In the case of a completely missing start date, the event will be considered to have started On-treatment unless an end date for the AE is provided which is before start of investigational product; in such a case the AE is assigned as Pre-treatment.
- If the IP Stop Date is missing, then any event with a start date on or after IP Start Date will be considered to be On-treatment.
  If the start date of the AE is after IP Stop Date but has been recorded as potentially related to IP, then it will be classified as On-treatment.

11.3.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Emergent	Emergent refers to AE Severity/ Lab toxicity that develops or increases in intensity after baseline

NOTES:

- If the study treatment stop date is missing, then the AE/ Lab toxicity will be considered to be On-Treatment unless an end date for the AE/ Lab toxicity is provided which is before start of investigational product; in such a case the AE/ Lab toxicity is assigned as Pre-treatment.
- Time of study treatment dosing and start/stop time of AEs/ Lab toxicity should be considered, if collected.

11.4. Appendix 4: Data Display Standards & Handling Conventions

11.4.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: uk1salx00175
HARP Compound	: \ARPROD\GSK2619619\ING200336\Documents*final_01(SAC)*
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1 or above). • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented as SDTM.	
Generation of RTF Files	
• RTF files will be generated for all reporting efforts.	

11.4.2. Reporting Standards

General

• The current GSK Statistical Display Standards in the GSK Standards Library (IDSL) will be applied for reporting, unless otherwise stated (Library Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics

Formats
• GSK Statistical Display Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected, unless otherwise stated. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the GSK Standard Statistical Display Principles but may be adjusted to a clinically interpretable number of DP's.
Planned and Actual Time

• Reporting for tables, figures and formal statistical analyses:
  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to GSK Standard Statistical Display Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the participant's listings.

Unscheduled Visits	
• Unscheduled visits will be included in listings. • Unscheduled visits will be assigned to a study visit using the all-inclusive windows defined in Section 11.2.1	
Descriptive Summary Statistics	
Continuous Data	Refer to GSK Standard Statistical Display Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to GSK Standard Statistical Display Principals 7.01 to 7.13.	

11.4.3. Reporting Standards for Pharmacokinetic

Pharmacokinetic Concentration Data	
PC Windows Non-Linear (WNL) File	PC WNL file (CSV format) for the non-compartmental analysis by Clinical Pharmacology Modelling and Simulation function will be created according to Standards for the Transfer and Reporting of PK Data document.
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to the GSK Standard PK Display Standard. Refer to the GSK Standard Statistical Display Principle 6.06.1. Note: If any concentration value is not calculable because of NQs, it will be excluded (set to missing) from the PK concentration Summary tables and Graphical displays and show as NQ in Listings. Refer to VQD-GUI-000722 (6.0) (Non-Compartmental Analysis of Pharmacokinetic Data) for handling of values below the Quantification Limit.
Pharmacokinetic Parameter Derivation	
PK Parameter to be Derived by Programmer	The PK parameters will be calculated by standard non-compartmental analysis according to current working practices and using WinNonLin v 5.2 or above. All calculations of non-compartmental parameters will be based on actual sampling times.
Pharmacokinetic Parameter Data	
Is NQ impacted PK Parameters Rule Being Followed	If any PK parameter is not calculable because of NQs, it will be excluded (set to missing) from the PK parameter summary. Refer to VQD-GUI-000722 (6.0) (Non-Compartmental Analysis of Pharmacokinetic Data) for handling of values below the Quantification Limit.
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to GSK Standard PK Display Standard.
Untransformed PK parameter	tmax (TMAX), t1/2

11.5. Appendix 5: Derived and Transformed Data

11.5.1. General

Multiple Measurements at One Analysis Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • If there are two values within a time window (as per Section 11.2.1) the value closest to the target day for that window will be used. If values are the same distance from the target, then the mean will be taken. • Participants having both High and Low values for Normal Ranges at any post-baseline visit for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

• Calculated as the number of days from initial study treatment start date:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < Treatment Start Date → Study Day = Ref Date –Treatment Start Date
  • Ref Data ≥ Treatment Start Date → Study Day = Ref Date – (Treatment Start Date) + 1
  • Note that Treatment Start Date is considered to be on Study Day 1 and the day before this is Study Day -1; i.e., there is no Study Day 0.

Post Baseline
• Post-baseline refers to the combined time periods of On-treatment and Post-treatment. Post-baseline may be further specified according to phase of the study: Antepartum, Delivery, Postpartum or Continuation.

11.5.2. Study Population

Extent of Exposure
• Number of days of exposure to study drug will be calculated based on the formula: • Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 1 • Participants who were randomized but did not report a treatment start date will be categorised as having zero days of exposure. • The cumulative dose will be based on the formula: • Cumulative Dose = Sum of (Number of Days x Total Daily Dose) • If there are any treatment breaks during the study, exposure data will be adjusted accordingly.
Demographics
Age
• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows: ○ Since only year of birth is recorded for subjects (day and month are not recorded), for the purpose of calculating age, day and month of birth will be imputed as '30th June'.

11.5.3. Efficacy

HIV-1 RNA
• Plasma for quantitative HIV-1 RNA will be collected. Methods to be used may include but are not limited to the Abbott RealTime HIV-1 Assay lower limit of detection (LLOD) 40 c/mL. In some cases (e.g., where the HIV-1 RNA is below the LLOD for a given assay) additional exploratory methods may be used to further characterize HIV-1 RNA levels.

Lymphocyte
CD4+ Cell Count
• Absolute CD4+ lymphocyte counts will be collected for assessment by flow cytometry.

11.5.4. Safety

Adverse Events
AE Severity – DAIDS Grading.
• The DAIDS grading for severity of clinical adverse events will be performed. • See protocol for DAIDS grading criteria.
Suicidality Monitoring
• Treatment emergent assessment of suicidality will be monitored during this study using the Columbia Suicide-Severity Rating Scale.

Laboratory Parameters
Lab Toxicities – DAIDS Grading
• The DAIDS grading for severity of clinical adverse events will be performed. • See protocol for DAIDS grading criteria

Laboratory Parameters
• If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, the number of significant digits in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value. o Example 1: 2 Significant Digits = '< x ' becomes x – 0.01 o Example 2: 1 Significant Digit = '> x' becomes x + 0.1 o Example 3: 0 Significant Digits = '< x' becomes x – 1

11.5.5. Pharmacokinetic

PK Parameters
• The PK Population will include all subjects who undergo PK sampling and have evaluable PK assay results. • See Table 5 for derived Pharmacokinetic parameters

11.6. Appendix 6: Reporting Standards for Missing Data

11.6.1. Premature Withdrawals

Element	Reporting Detail
• General	• Participant study completion (i.e. as specified in the protocol) was defined as: Subjects are considered to have completed the study after completing the postpartum evaluation. • Withdrawn participants were not replaced in the study. • All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables, listings and figures, unless otherwise specified.

11.6.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: o These data will be indicated by the use of a "blank" in participant listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.
Outliers	• Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

11.6.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays.
Adverse Events	• Imputations in the adverse events dataset are used for slotting events to the appropriate study time periods and for sorting in data listings. • Partial dates for AE recorded in the CRF will be imputed using the following conventions:

Missing start day	• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = 1st of month. • Else if study treatment start date is not missing: o If month and year of start date = month and year of study treatment start date then ▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date= 1st of month. ▪ Else set start date = study treatment start date. o Else set start date = 1st of month.
Missing start day and month	• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = January 1. • Else if study treatment start date is not missing: o If year of start date = year of study treatment start date then

<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
<tr><td></td><td>
<table>
<tr><td></td><td>▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date = January 1.
▪ Else set start date = study treatment start date.
o Else set start date = January 1.</td></tr>
<tr><td>Missing stop day</td><td>Last day of the month will be used.</td></tr>
<tr><td>Missing stop day and month</td><td>No Imputation</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table>
• Completely missing start or end dates will remain missing, with no imputation applied.
</td></tr>
<tr><td>Concomitant Medications/ Medical History</td><td>
• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention:
<table>
<tr><td>Missing start day</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = 1st of month.
• Else if study treatment start date is not missing:
o If month and year of start date = month and year of study treatment start date then
▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date= 1st of month.
▪ Else set start date = study treatment start date.
o Else set start date = 1st of month.</td></tr>
<tr><td>Missing start day and month</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = January 1.
• Else if study treatment start date is not missing:
o If year of start date = year of study treatment start date then
▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date = January 1.
▪ Else set start date = study treatment start date.
• Else set start date = January 1.</td></tr>
<tr><td>Missing end day</td><td>A '28/29/30/31' will be used for the day (dependent on the month and year)</td></tr>
<tr><td>Missing end day and month</td><td>A '31' will be used for the day and 'Dec' will be used for the month.</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation</td></tr>
</table>
• The recorded partial date will be displayed in listings.
</td></tr>
</table>

11.7. Appendix 7: Values of Potential Clinical Importance

11.7.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	Ratio of 1			0.54
		Δ from BL	-0.075	
Haemoglobin	g/L			180
		Δ from BL	-25	
Lymphocytes	$x10^9$/ L		0.8	
Neutrophil Count	$x10^9$/ L		1.5	
Platelet Count	$x10^9$/ L		100	550
While Blood Cell Count (WBC)	$x10^9$/ L		3	20

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	g/L		<30	
Calcium	mmol/L		2	2.75
Creatinine	umol/L	Δ from BL		44.2
Glucose	mmol/L		3	9
Magnesium	mmol/L		<0.5	>1.23
Phosphorus	mmol/L		<0.8	>1.6
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150
Total CO2	mmol/L		<18	>32

11.7.2. Vital Signs

Vital Sign Parameter (Absolute)	**Units**	**Clinical Concern Range**	
		Lower	**Upper**
Systolic Blood Pressure	mmHg	<85	>160
Diastolic Blood Pressure	mmHg	<45	>100
Heart Rate	bpm	<40	>110

11.8. Appendix 8: Abbreviations & Trademarks

11.8.1. Abbreviations

Abbreviation	Description
ABC	Abacavir
ADaM	Analysis Data Model
AE	Adverse Event
AGA	Appropriate for Gestational Age
A&R	Analysis and Reporting
APGAR	Appearance, Pulse rate, Grimace, Activity, Respiration
CDISC	Clinical Data Interchange Standards Consortium
CD4+	Helper-inducer T-lymphocyte having surface antigen CD4 (cluster of differentiation 4)
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
CSR	Clinical Study Report
C-SSRS	Columbia Suicide Severity Rating Scale
DAIDS	Division of AIDS
DBF	Database Freeze
DBR	Database Release
DTG	Dolutegravir
eCRF	Electronic Case Record Form
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
FDC	Fixed Dose Combination
GSK	GlaxoSmithKline
IA	Interim Analysis
ICH	International Conference on Harmonization
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library (GSK Standards Library)
IMMS	International Modules Management System
IP	Investigational Product
ITT(E)	Intent-To-Treat (Exposed)
IUGR	Intrauterine Growth Restriction
LGA	Large for Gestational Age
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
RAP	Reporting & Analysis Plan
RNA	Ribonucleic acid
SAC	Statistical Analysis Complete
SAS	Statistical Analysis Software
SDTM	Study Data Tabulation Model
SGA	Small for Gestational Age

11.8.2. Trademarks

Trademarks of the ViiV Healthcare
Dolutegravir
Epzicom/Kivexa

Trademarks not owned by the ViiV Healthcare
SAS
WinNonlin

11.9. Appendix 9: List of Data Displays

All data displays will use the term "subject" rather than "participant" in accordance with CDSIC and GSK Statistical Display Standards.

11.9.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.n	NA
Efficacy	2.1 to 2.n	NA
Safety	3.1 to 3.n	NA
Pharmacokinetic	4.1 to 4.n	4.1 to 4.n
Virology	5.1	NA
Maternal and Infant Assessment	6.1 to 6.n	NA
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

11.9.2. Mock Example Shell Referencing

Nonstandard specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 9: Example Mock Shells for Data Displays.

Section	Table	Listing
Pharmacokinetic	PK_Tn	PK_Ln
Maternal Outcomes	MAT_Tn	MAT_Ln
Infant Outcomes	INF_Tn	INF_Ln
Virology	VIR_Tn	NA

- **NOTES:** For displays having Example shell as *, refer to TANGO Study (Compound: GSK3515864, Study ID: 204862, Reporting Effort: primary_01)

11.9.3. Deliverables

Delivery [Priority]	Description
IA SAC	Interim Analysis Statistical Analysis Complete

11.9.4. Study Population Tables

Study Population Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	ITT-E	ES1	Summary of Subject Disposition for the Subject Conclusion Record overall and by relationship to COVID-19 Pandemic	Table will be summarised overall and then by COVID-19 relationship	IA SAC
1.2.	Enrolled	NS3	Summary of Number of Subjects by Country and Site ID	EudraCT/Clinical Operations	IA SAC
Demographic and Baseline Characteristics					
1.3.	ITT-E	DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	IA SAC
1.4.	Enrolled	DM11	Summary of Age Ranges	EudraCT	IA SAC
1.5.	ITT-E	DM6	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	IA SAC

11.9.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Plasma HIV-1 RNA					
2.1	ITT-E	*	Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL by Visit		IA SAC
2.2	ITT-E	*	Proportion of Subjects with Plasma HIV-1 RNA <400 c/mL by Visit		IA SAC

Efficacy: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.3	ITT-E	*	Summary of Change from Baseline in HIV-1 RNA (c/mL) by Visit		IA SAC
CD4+ Cell Count					
2.4	ITT-E	*	Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit		IA SAC
Post- Baseline Disease Progression					
2.5	ITT-E	*	Summary of Post-Baseline HIV-1 Disease Progressions		IA SAC

11.9.6. Safety Tables

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	Safety	AE5B	Summary of All Adverse Events by System Organ Class, Preferred term and Maximum Toxicity	Ct.gov	IA SAC
3.2.	Safety	AE3	Summary of Grade 2-4 Adverse Events by Overall Frequency	ICH E3	IA SAC

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.3.	Safety	AE15	Summary of Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT	IA SAC
3.4.	Safety	AE3	Summary of Non-Serious Drug-Related Adverse Events by Overall Frequency	Plain Language Summary requirements (PLS).	IA SAC
3.5.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT	IA SAC

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.6.	Safety	AE20	Summary of Serious Fatal and Non-Fatal Drug-Related Adverse by Overall Frequency	Plain Language Summary requirements (PLS).	IA SAC
3.7.	Safety	AE8	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study		IA SAC
3.8.	Safety	*	Summary of Maximum Post-Baseline Emergent Chemistry Toxicities	The key parameters would include ALT, AST, Total bilirubin, serum creatinine and GFR	IA SAC
3.9.	Safety	*	Summary of Maximum Post-Baseline Emergent Hematology Toxicities	The parameters would include Hemoglobin, platelets, WBC	IA SAC

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.10.	Safety	LB1	Summary of Chemistry Changes from Baseline by Visit	The key parameters would include ALT, AST, Total bilirubin, serum creatinine and GFR	IA SAC
3.11.	Safety	LB1	Summary of Hematology Changes from Baseline by Visit	The parameters would include Hemoglobin, platelets, WBC	IA SAC
3.12.	Safety	LB1	Summary of Urinalysis Changes from Baseline by Visit	Key parameters would be Urine protein/Creatinine ratio and Urine/Protein ratio	IA SAC

11.9.7. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
DTG PK					
4.1.	PK	PK01	Summary of Plasma DTG PK Concentration-Time Data by Visit and Nominal Time Relative to Dose		IA SAC
4.2.	PK	PK_T1	Summary of untransformed and loge-transformed Derived Plasma DTG PK Parameters		IA SAC

11.9.8. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
DTG PK					
4.1.	PK	PK24	Individual Plasma DTG Concentration-Time Plots (linear and Semi-log)		IA SAC
4.2.	PK	PK17	Mean Plasma DTG Concentration-Time plots (linear and semi-log)		IA SAC
4.3.	PK	PK18	Median Plasma DTG Concentration-Time plots (linear and semi-log)		IA SAC

11.9.9. Virology Tables

Virology: Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.1	ITT-E	VIR_T1	Summary of Incidence of treatment-emergent genotypic and/or phenotypic resistance in subjects who meet confirmed virologic withdrawal criteria		IA SAC

11.9.10. Maternal and Infant Assessment Tables

Maternal and Infant Outcomes: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.1	Safety	MAT_T1	Summary of Maternal Outcomes		IA SAC
6.2	Safety	INF_T1	Summary of Infant Outcomes at Birth		IA SAC

11.9.11. ICH Listings

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	ITT-E	ES2	Listing of Reasons for Study Withdrawal	ICH E3	IA SAC
Protocol Deviations					
2.	ITT-E	DV2	Listing of Important Protocol Deviations	ICH E3	IA SAC
3.	ITT-E	DV2	Listing of all non-Important COVID-19 related Protocol Deviations		IA SAC
Demographic and Baseline Characteristics					
4.	ITT-E	DM2	Listing of Demographic Characteristics	ICH E3	IA SAC
5.	ITT-E	DM9	Listing of Race	ICH E3	IA SAC
Exposure and Treatment Compliance					
6.	ITT-E	EX3	Listing of Investigational Product Exposure Data	ICH E3	IA SAC
Adverse Events					
7.	Safety	AE8	Listing of All Adverse Events	ICH E3	IA SAC

ICH: Listings					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Serious and Other Significant Adverse Events					
8.	Safety	AE8CPA	Listing of Non-Fatal Serious Adverse Events	ICH E3	IA SAC
9.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	IA SAC
10.	Safety	AE8	Listing of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study	ICH E3	IA SAC
Laboratory Assessments					
11.	Safety	LB5	Listing of Clinical Chemistry Laboratory Data	ICH E3	IA SAC
12.	Safety	LB5	Listing of Haematology Laboratory Data	ICH E3	IA SAC
13.	Safety	UR2	Listing of Urinalysis Data	ICH E3	IA SAC

11.9.12. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Prior and Concomitant Medications					
14.	ITT-E	CM3	Listing of Concomitant Medications		IA SAC

Non-ICH: Listings					
No.	**Population**	**Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
15.	ITT-E	CM3	Listing of Prior ART Medications	Not Required	
16.	ITT-E	CM3	Listing of Concomitant ART Medications		IA SAC
17.	ITT-E	*	Listing of Relationship Between ATC Level 1, Ingredient and Verbatim Text		IA SAC
18.	ITT-E	*	Listing of Relationship Between ATC Level 4, Ingredient and Verbatim Text		IA SAC
Adverse Events					
19.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		IA SAC
Pandemic					
20.	Safety	PAN12	Listing of COVID-19 Assessments and Symptom assessments		IA SAC

Non-ICH: Listings					
No.	**Population**	**Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Non-Laboratory values					
21.	Safety	ECSSRS4	Listing of C-SSRS Suicidal Ideation and Behaviour Data		IA SAC
Subject Disposition					
22.	ITT-E	*	Listing of Investigational Product Accountability		IA SAC
23.	ITT-E	TA1	Listing of Planned and Actual Treatments		
24.	All Subjects Screened	*	Listing of Study Populations		IA SAC
25.	Enrolled	*	Listing of Subject Recruitment by Country and Site Number	Add a column “ARIA-ING117172 Unique Subject ID”	IA SAC
26.	ITT-E	*	Listing of Visit Dates		IA SAC
27.	ITT-E	CDC3	Listing of CDC Classification of HIV Infection at Baseline		IA SAC
28.	ITT-E	RF2	Listing of HIV Risk Factors		IA SAC
Medical Conditions					
29.	ITT-E	MH2	Listing of Current and Past Medical Conditions at Baseline		IA SAC
Baseline Characteristics					
30.	ITT-E	*	Listing of Baseline Cardiovascular Risk Assessment Data		IA SAC
31.	ITT-E	*	Listing of History of Cardiac Therapeutic Procedures		IA SAC
32.	ITT-E	*	Listing of Cardiovascular Events at Baseline		IA SAC
33.	ITT-E	MAT_L2	Listing of Maternal History		IA SAC
Efficacy					
34.	ITT-E	*	Listing of Quantitative Plasma HIV-1 RNA		IA SAC

Non-ICH: Listings					
No.	**Population**	**Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
35.	ITT-E	*	Listing of CD4+ Cell Count Data		IA SAC
Vital Signs					
36.	Safety	VS4	Listing of All Vital Signs Data		IA SAC
PK Endpoints					
37.	PK	PK_L1	Listing of Plasma DTG PK Concentration-Time Data		IA SAC
38.	PK	PK_L2	Listing of Plasma DTG PK Parameters		IA SAC
Maternal and Infant Endpoints					
39.	Safety	MAT_L1	Listing of Maternal Outcomes		IA SAC
40.	Safety	MAT_L3	Listing of Pregnancy Risk Assessment		IA SAC
41.	Safety	INF_L1	Listing of Infant Outcomes		IA SAC

11.10. Appendix 10: Example Mock Shells for Data Displays

Example mock shells for Data Displays will be provided in a separate document.