Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)
Title	:	Open-Label, Single-Sequence Study to Evaluate the Effects of Darunavir/Ritonavir and/or Etravirine on the Pharmacokinetics of GSK3640254 and the Effects of GSK3640254 on the Pharmacokinetics of Darunavir/Ritonavir and/or Etravirine in Heathy Adults
Compound Number	:	GSK3640254
Effective Date	:	15/10/2021

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report (CSR) for Protocol 213054.
- This RAP is intended to describe the full 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) deliverable.

TABLE OF CONTENTS

PAGE

1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the CSR for Protocol: 213054.

2. SUMMARY OF KEY PROTOCOL INFORMATION

This is an open-label, single-sequence, multiple-dose, 3 cohort study.

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Version / Release Date	Summary of Changes
Final 1.0 / 2021-02-24	
Final 2.0 / 2021-10-15	• Add Enrolled population as " All participants who passed screening and entered the study " for the presentation of .disposition analysis (Data display 1.1). • In Section 5.2, change baseline for Cohort 3 Period 2 to Day 1 (Pre-Dose).

2.2. Study Objective(s) and Endpoint(s)

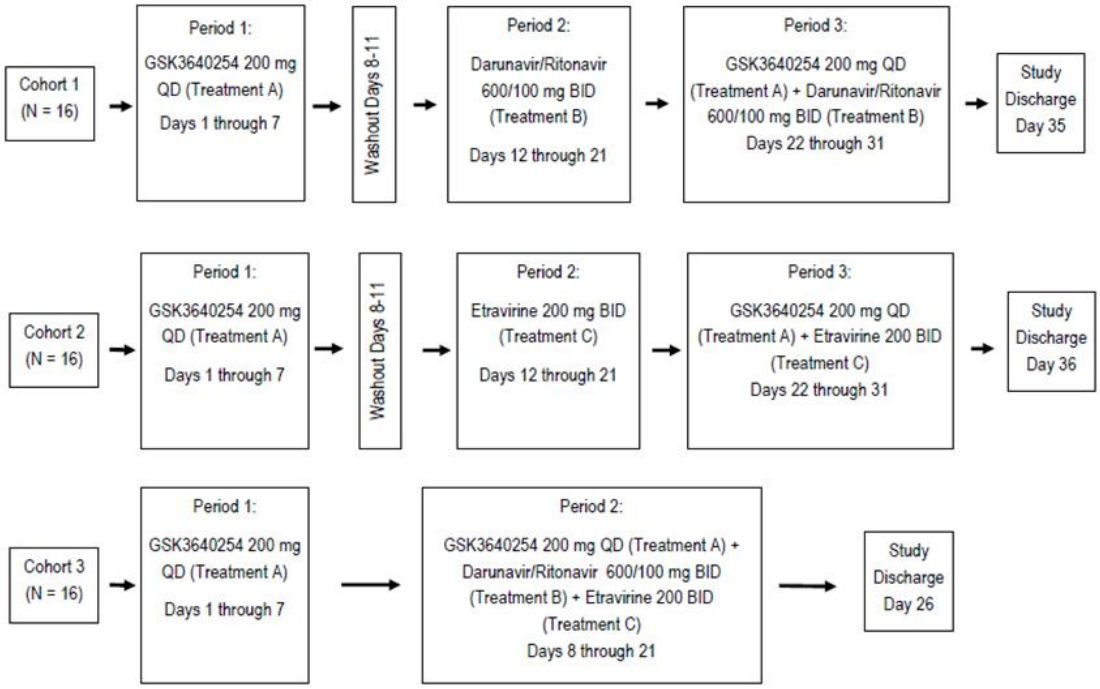
	Objectives	Endpoints
	Primary	
Cohort 1	• To assess the effect of co-administration of DRV/ RTV 600/100 mg BID with GSK3640254 200 mg QD on the PK of GSK3640254 in healthy participants. • To assess the effect of co-administration of GSK3640254 200 mg QD with DRV/RTV 600/100 mg BID on the PK of DRV/RTV in healthy participants.	• AUC(0-tau) and Cmax for GSK3640254 • AUC(0-tau), and Cmax for DRV/RTV
Cohort 2	• To assess the effect of co-administration of ETR 200 mg BID with GSK3640254 200 mg QD on the PK of GSK3640254 in healthy participants. • To assess the effect of co-administration of ETR 200 mg BID with GSK3640254 200 mg QD on the PK of ETR in healthy participants.	• AUC(0-tau) and Cmax for GSK3640254 • AUC(0-tau), and Cmax for ETR
Cohort 3	• To assess the effect of co-administration of ETR 200 mg BID and DRV/RTV 600/100 mg BID with GSK3640254 200 mg QD on the PK of GSK3640254 in healthy participants.	• AUC(0-tau) and Cmax for GSK3640254

	Secondary	
Cohort 1	• To assess the effect of co-administration of GSK3640254 200 mg QD with DRV/RTV 600/100 mg BID on the secondary PK parameters of DRV and RTV in healthy participants.	• Ctau, and Tmax for DRV, RTV, and GSK3640254
Cohort 2	• To assess the effect of co-administration of GSK3640254 200 mg QD with ETR 200 mg BID on the secondary PK parameters of ETR in healthy participants.	• Ctau, and Tmax for ETR, and GSK3640254
Cohort 1, 2 & 3	• To assess the safety and tolerability of GSK3640254 administered alone and in combination with DRV/RTV and/or ETR.	• Safety and tolerability endpoints include incidence of AEs, SAEs, AEs leading to discontinuation, deaths, marked laboratory abnormalities, and abnormalities in vital signs and 12-lead ECGs.

AE = adverse event; AUC(0-tau) = area under the plasma concentration-time curve from time zero to the end of the dosing interval at steady state; BID = twice daily; DRV = darunavir; Cmax = maximum observed concentration, Ctau = plasma concentration at the end of the dosing interval; ECG = electrocardiogram; ETR = etravirine; PK = pharmacokinetics; QD = once daily; RTV = ritonavir; SAE = serious adverse event; Tmax = time of maximum observed concentration.

2.3. Study Design

Overview of Study Design and Key Features



BID = twice daily; N = number of participants; QD = once daily.

Design Features	A Phase 1, single-sequence, multiple-dose, 3 cohort study.
	The study will consist of a screening period and a treatment period.
	• Screening Period: within 28 days before the first dose of study intervention
	• Treatment Period – Cohort 1
	  ▪ Period 1: GSK3640254 200 mg tablets QD (Treatment A) on Days 1 through 7.
	  ▪ Period 2: Darunavir (DRV)/ Ritonavir (RTV) 600/100 mg tablets twice daily (BID) (Treatment B) on Days 12 through 21.
	  ▪ Period 3: GSK3640254 200 mg tablets once daily (QD) (Treatment A) and DRV/RTV 600/100 mg tablets BID (Treatment B) on Days 22 through 31.
	• Treatment Period – Cohort 2
	  ▪ Period 1: GSK3640254 200 mg tablets QD (Treatment A) on Days 1 through 7.
	  ▪ Period 2: Etravirine (ETR) 200 mg tablets BID (Treatment C) on Days 12 through 21.
	  ▪ Period 3: GSK3640254 200 mg tablets QD (Treatment A) and ETR 200 mg tablets BID (Treatment C) on Days 22 through 31.
	• Treatment Period – Cohort 3
	  ▪ Period 1: GSK3640254 200 mg tablets QD (Treatment A) on Days 1 through 7.
	  ▪ Period 2: GSK3640254 200 mg tablets QD (Treatment A), DRV/RTV 600/100 mg tablets BID (Treatment B), and ETR 200 mg tablets BID

Overview of Study Design and Key Features	
	(Treatment C) on Days 8 through 21. Per cohort, approximately 16 participants will be treated to ensure that 14 evaluable participants complete the study.
Dosing	• Treatment A: GSK3640254 200 mg tablets QD • Treatment B: DRV/RTV 600/100 mg tablets BID • Treatment C: ETR 200 mg tablets BID
Time & Events	• Refer to Appendix 1: Schedule of Activities
Treatment Assignment	• PPD Clinical Pharmacology will remain open—label throughout the study.First 16 participants will be assigned to Cohort 3, and remaining 32 participants will be randomly assigned to Cohort 1 or 2.
Interim Analysis	• No interim analysis is planned for this study

2.4. Statistical Hypotheses

There is no formal hypothesis that will be statistically tested in this study.

Administration of GSK3640254 may change the exposure to DRV/RT and ETR, and administration of DRV/RTV and ETR may change the exposure to GSK3640254.

2.5. Sample Size Determination

As there is no formal research hypothesis being statistically tested in this study, the sample size was not selected based on statistical considerations but determined using feasibility. Per cohort, approximately 16 participants will be enrolled to ensure that 14 evaluable participants complete the study. If participants prematurely discontinue the study, additional participants may be enrolled after consultation with the sponsor to ensure that the required number of evaluable participants complete the study.

3. PLANNED ANALYSES

3.1. Final Analyses

The final planned primary analyses will be performed after the completion of the following sequential steps:

1. All participants have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database release (DBR) and database freeze (DBF) have been declared by Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who signed the informed consent form.	• Study Population
Enrolled	• All participants who passed screening and entered the study	• Disposition
Randomized	• All participants who are randomly assigned to a cohort.	• Disposition
Safety	• The Safety Population will include all participants who receive at least 1 dose of study medication. Participants will be analyzed according to the intervention they actually received.	• Demographic • Safety
Pharmacokinetic Concentration	• The PK Concentration Population will include all participants who undergo plasma PK sampling and have evaluable PK assay results.	• PK Concentration
Pharmacokinetic Parameter	• The PK Parameter Population will include all participants who undergo plasma PK sampling and have at least 1 evaluable PK parameter estimated.	• PK Parameter • PK statistical analysis

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

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, participant management, or participant assessment) will be summarized and listed.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Study Deviation Tool and Rules. The "significant" protocol deviation in the Study Deviation Tool and Rules is equivalent to "important" protocol deviations.

- Data will be reviewed prior to freezing the database to ensure all significant deviations and deviations which may lead to exclusion from the analysis are captured and categorised on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

A separate listing of all inclusion/exclusion criteria deviations will also be provided. This listing will be based on data as recorded on the inclusion/exclusion page of the electronic case record form (eCRF).

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
Data Displays for Reporting			
Description	**Code**	**Order in TLF**	**Cohort Used**
GSK3640254 200 mg tablets QD on Days 1 through 7.	Treatment A	1	Cohorts 1, 2, 3
DRV/RTV 600/100 mg tablets twice daily (BID) (Treatment B) on Days 12 through 21.	Treatment B	2	Cohort 1
GSK3640254 200 mg tablets QD and DRV/RTV 600/100 mg tablets BID on Days 22 through 31.	Treatment A + Treatment B	3	Cohort 1
ETR 200 mg tablets BID on Days 12 through 21.	Treatment C	4	Cohort 2
GSK3640254 200 mg tablets QD and ETR 200 mg tablets BID on Days 22 through 31.	Treatment A + Treatment C	5	Cohort 2
GSK3640254 200 mg tablets QD, DRV/RTV 600/100 mg tablets BID, and ETR 200 mg tablets BID on Days 8 through 21.	Treatment A + Treatment B +Treatment C	6	Cohort 3

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions), baseline is defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits.

Cohorts 1 and 2:

Parameter	Study Assessments Considered as Baseline					Baseline Used in Data Display		
	Check-in (Day -2)	Baseline (Day -1)	Day 1 (Pre-dose)	Day 12 (Pre-dose)	Day 22 (Pre-dose)	Period 1	Period 2	Period 3 & Follow-up
Vital Sign	X	X	X	X	X	Day 1 (Pre-Dose)[1]	Day 12 (Pre-Dose)[1]	Day 22 (Pre-Dose)[1]
12-Lead ECG	X	X	X	X	X	Day 1 (Pre-Dose)[1]	Day 12 (Pre-Dose)[1]	Day 22 (Pre-Dose)[1]

[1] The average (for blood pressure, pulse, and ECG numeric assessment) or the worst case (for ECG interpretation - Normal> Abnormal, Not Clinical Significant> Abnormal, Clinically Significant) of the pre-dose triplicate assessments will be used as the baseline.

Cohort 3:

Parameter	Study Assessments Considered as Baseline				Baseline Used in Data Display	
	Check-in (Day -2)	Baseline (Day -1)	Day 1 (Pre-dose)	Day 8 (Pre-dose)	Period 1	Period 2 and follow-up
Vital Sign	X	X	X	X	Day 1 (Pre-Dose)[1]	Day 8 (Pre-Dose)[1]
12-Lead ECG	X	X	X	X	Day 1 (Pre-Dose)[1]	Day 1 (Pre-Dose)[1]

[1] The average (for blood pressure, pulse, and ECG numeric assessment) or the worst case (for ECG interpretation - Normal> Abnormal, Not Clinical Significant> Abnormal, Clinically Significant)) of the pre-dose triplicate assessments will be used as the baseline

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

5.3. 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
10.1	Appendix 1: Schedule of Activities
10.2	Appendix 2: Study Phase and Treatment Emergent Adverse Event
10.3	Appendix 3: Data Display Standards & Handling Conventions
10.4	Appendix 4: Derived and Transformed Data
10.5	Appendix 5: Reporting Standards for Missing Data
10.6	Appendix 6: Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events
10.7	Appendix 7: Values of Potential Clinical Importance

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the “Safety”, “Randomized” or “Screened”, population, unless otherwise specified.

Study population analyses including analyses of participant’s disposition, protocol deviations (including inclusion/exclusion criteria deviations), demographic and baseline characteristics, prior and concomitant medications, and exposure will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 9: List of Data Displays.

7. PHARMACOKINETIC ANALYSES

7.1. Primary Pharmacokinetic Analyses

7.1.1. Endpoint / Variables

7.1.1.1. Drug Concentration Measures

Refer to Appendix 3: Data Display Standards & Handling Conventions (Section 10.3.3 Reporting Standards for PK). Plasma concentrations of GSK3640254, DRV, RTV, and ETR will be measured and presented in tabular form and will be summarized descriptively. Plasma GSK3640254, DRV, RTV, and ETR concentration-time data will be listed by participant, treatment group, and sampling time and summarized by treatment group and sampling time.

7.1.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin (8.0 or higher). All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data, as data permits. Subjects who experience emesis at or before 2 times median T_{max} for the given treatment will be excluded from the calculation of summary statistics and statistical analysis for the respective treatment.

Parameter	Parameter Description
Cmax	Maximum observed concentration, determined directly from the concentration-time data.
AUC(0-tau)	Area under the plasma concentration-time curve from time 0 to the end of the dosing interval at steady state, to be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.

NOTES:
- Additional parameters may be included as required.

7.1.2. Summary Measure

Pharmacokinetic parameters AUC(0-tau) and Cmax following administration of GSK3640254 with or without administration of DRV/RTV and/or ETR to healthy participants.

7.1.3. Population of Interest

The primary PK analyses will be based on the PK concentration population for plasma PK concentrations and the PK parameter population for plasma PK parameters and statistical analysis.

7.1.4. 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 7.1.1 will be summarized using descriptive statistics, graphically presented (where appropriate), and listed.

Primary plasma PK parameters (AUC[0-tau] and Cmax) will be estimated for GSK3640254, DRV, RTV, and ETR. Summary statistics (arithmetic mean, geometric mean, median, standard deviation [SD], minimum, maximum, between-subject coefficient of variation [CVb], and 95% CI for plasma PK parameter values) will be summarized by treatment.

7.1.4.1. Statistical Methodology Specification

The following PK statistical analyses will only be performed if sufficient data are available (i.e. if participants have well defined plasma profiles).

Endpoint / Variables
• Plasma primary PK endpoints include AUC(0-tau) and Cmax, as data permit
Model Specification
• Analysis will be performed to compare the PK exposure of GSK3640254 with and without DRV/RTV (Cohort 1), ETR (Cohort 2), or DRV/RTV/ETR (Cohort 3). Analyses will be performed on the natural logarithms of AUC(0-tau) and Cmax using linear mixed-effect models with treatment as a fixed effect, and measurements within participant as repeated measures, and subject as a random effect. • Effects will be estimated, and CIs will be constructed for the following treatment comparisons: Treatment A+B versus Treatment A (Cohort 1) Treatment A+C versus Treatment A (Cohort 2) Treatment A+B+C versus Treatment A (Cohort 3) • Point estimates and 90% CIs for treatment differences on the log scale derived from the model will be exponentiated to obtain estimates for geometric mean ratios and CIs on the original scale. • Analysis will be performed to compare the PK exposure of DRV (Cohort 1), RTV (Cohort 1), and ETR (Cohort 2) with and without GSK3640254. Analyses will be performed on the natural logarithms of AUC(0-tau) and Cmax using linear mixed-effect models with treatment as a fixed effect, and measurements within participant as repeated measures, and subject as a random effect. • Effects will be estimated, and CIs will be constructed for the following treatment comparisons: Treatment A+B versus Treatment B (Cohort 1) Treatment A+C versus Treatment C (Cohort 2) • Point estimates and 90% CIs for treatment differences on the log scale derived from the model will be exponentiated to obtain estimates for geometric mean ratios and CIs on the original scale.
Model Checking & Diagnostics
• • Model assumptions will be applied, but appropriate adjustments may be made based on the data.
Model Results Presentation
• Statistical analysis by analysis of variance (ANOVA) will be presented in tabular format with geometric mean ratios and 90% CIs for: Treatment A+B versus Treatment A (Cohort 1) Treatment A+C versus Treatment A (Cohort 2)

Treatment A+B+C versus Treatment A (Cohort 3)

- Statistical analysis by analysis of variance (ANOVA) will be presented in tabular format with geometric mean ratios and 90% CIs for:
  Treatment A+B versus Treatment B (Cohort 1)
  Treatment A+C versus Treatment C (Cohort 2)

7.2. Secondary Pharmacokinetic Analyses

7.2.1. Endpoint / Variables

7.2.1.1. Drug Concentration Measures

Refer to Appendix 3: Data Display Standards & Handling Conventions (Section 10.3.3 Reporting Standards for PK)

7.2.1.2. Derived Pharmacokinetic Parameters

Plasma PK parameters listed below will be determined from the plasma concentration-time data, as data permits.

Parameter	Parameter Description
Tmax	Time of maximum observed concentration
Ctau	Plasma concentration at the end of the dosing interval

NOTES:

- Additional parameters may be included as required.

If additional pharmacokinetic parameters are needed they will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin (8.0 or higher). All calculations of non-compartmental parameters will be based on actual sampling times. Subjects who experience emesis at or before 2 times median T_{max} for the given treatment will be excluded from the calculation of summary statistics and statistical analysis for the respective treatment.

7.2.2. Summary Measure

Pharmacokinetic parameters Tmax and Ctau of GSK3640254, DRV, RTV, and ETR following administration of GSK3640254 with or without administration of DRV/RTV and/or ETR to healthy participants.

7.2.3. Population of Interest

The secondary PK analyses will be based on the PK concentration population for plasma PK concentrations, and the PK parameter population for plasma and statistical analysis, unless otherwise specified.

7.2.4. 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 7.1.1 will be summarized using descriptive statistics, graphically presented (where appropriate), and listed.

Secondary plasma PK parameters (Tmax and Ctau) will be estimated for GSK3640254, DRV, RTV and ETR. Summary statistics (arithmetic mean, geometric mean, median, SD, minimum, maximum, and coefficient of variation) for plasma PK parameter values will be summarized by treatment.

Additionally, pre-dose (trough) PK plasma concentrations of GSK3640254, DRV, RTV, and ETR will be summarized and used to assess achievement of steady state.

8. SAFETY ANALYSES

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

8.1. Adverse Events Analyses

Adverse events (AEs) analyses including the analysis of AEs, serious AEs (SAEs), AEs of special interest (AESI), and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 9: List of Data Displays.

For studies with greater than one treatment period (e.g., crossover study), if AE onset is during one period and worsens during a later period, it will be counted in both periods. For the later period the onset date of AE with the elevated grade will be the first dose date of the later treatment period.

8.2. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of chemistry laboratory tests, hematology laboratory tests, urinalysis, liver function tests, and pregnancy test will be based on GSK Core Data Standards and will be graded using the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events (Version 2.1, July 2017).The details of the planned displays are in Appendix 9: List of Data Displays.

8.3. Adverse Events of Special Interest

At the end of the study, QT prolongation, gastrointestinal intolerability, gastric toxicity, psychiatric events, nervous system disorders, and skin and subcutaneous tissue disorders will be summarized by treatment. A listing will also be provided accordingly.

The AESI of QT prolongation will be defined as cardiac disorders system organ class (SOC) plus preferred terms (PTs) using the Medical Dictionary for Regulatory Activities (MedDRA) Standardized MedDRA Query (SMQ) “Torsade de pointes/QT Prolongation” (narrow and broad terms) plus seizure.

Gastrointestinal intolerability and gastric toxicity AESIs will be defined within three narrow sub-SMQs [Gastrointestinal nonspecific symptoms and therapeutic procedures SMQ; Gastrointestinal nonspecific dysfunction SMQ; Gastrointestinal nonspecific inflammation (SMQ)] plus a selection of relevant broad PTs from the Gastrointestinal non-specific symptoms and therapeutic procedures SMQ.

Psychiatric AESI will be defined within the following:

- Sub-SMQ “Suicide/self-injury” (SMQ) from parent SMQ of “Depression and Suicide/Self Injury”. Only narrow terms from the sub-SMQ will be selected.
- Sub-SMQ “Depression (excluding suicide and self-injury)” (SMQ) from parent SMQ of “Depression and Suicide/Self Injury”. Only narrow terms from the sub-SMQ will be selected.

- All PTs from high level group term (HLGT) "Manic and Bipolar Mood Disorders and Disturbances" under SOC "Psychiatric Disorders".
- Narrow terms from SMQ "Psychosis and Psychotic Disorders" selected.
- All PTs from HLGT "Anxiety Disorders and Symptoms", under SOC "Psychiatric disorders".
- All PTs from HLGT "Sleep Disorders and Disturbances" and HLGT "Sleep disturbances (include subtypes)".

Nervous system disorders AESIs will be defined within the following:

- Four HLGTs under Nervous System Disorders SOC: "Headaches"; "Mental impairment disorders (excluding dementia)"; "Disturbance in consciousness" and "Seizures and seizure disorder"

Skin and subcutaneous tissue disorder AESIs will be defined with the following PTs:

Dermatitis, Dermatitis allergic, Dermatitis atopic, Eczema, Eczema eyelids, Eczema nummular, Eyelid irritation, Skin irritation, Urticarial dermatitis, Eyelid pruritis, Pruritus, Pruritus allergic, Rash pruritic, Rash, Rash macular, Rash maculopapular, Rash morbilliform, Rash papular, Rash pruritic, Urticaria, Drug eruption and Rash pustular

8.4. Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs, vital signs, liver events, and Columbia Suicide Severity Rating Scale (C-SSRS) will be based on GSK Core Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 9: List of Data Displays.

8.5. COVID 19 Related Analyses

Based on GSK's "Impact of COVID-19 on Assessment of Safety in Clinical Trials Points to Consider", it is GSK's recommendation that study teams should capture COVID-19 cases based on the WHO criteria using the categories of: suspected, probable, and confirmed cases. COVID-19 eCRF pages are used in the study for data collection and analysis purposes. After a discussion with the study team, the following analyses will be included:

- Number of subjects with suspected, probable, or confirmed COVID-19 infection
- Number of subjects who had a COVID-19 diagnosis test performed and the number of subjects with positive, negative, or indeterminate results
- Incidence of COVID-19 as reported as an AE and SAE
- Incidence of treatment discontinuation due to an AE of COVID-19 infection
- Severity, duration, and outcome of COVID-19 AEs

If percentage of COVID-19 cases is >10% (> 5 subjects with an AE of COVID-19), a summary of COVID-19 symptoms for subjects with COVID-19 AE will be added.

Further display details are provided in Appendix 9: List of Data Displays.

9. REFERENCES

ViiV Healthcare group of companies Document Number 2020N432810_00 (10SEP2020) Open-Label, Single-Sequence Study to Evaluate the Effects of Darunavir/Ritonavir and/or Etravirine on the Pharmacokinetics of GSK3640254 and the Effects of GSK3640254 on the Pharmacokinetics of Darunavir/Ritonavir and/or Etravirine in Heathy Adults

10. APPENDICES

10.1. Appendix 1: Schedule of Activities

10.1.1. Protocol Defined Schedule of Events

Screening Visit

Procedure	Screening (up to 28 days before Day 1)
Outpatient visit	X
Informed consent	X
Inclusion and exclusion criteria	X
Demography	X
Full physical examination including height and weight [0]	X
Laboratory assessments (hematology, clinical chemistry, urinalysis)	X
12-lead electrocardiogram	X
Vital sign measurements	X
Medication/drug/alcohol history	X
Past and current medical conditions	X
Columbia-Suicide Severity Rating Scale	X
Serum pregnancy test	X
Follicle-stimulating hormone (as needed, to confirm postmenopausal status)	X
Drug, alcohol, and cotinine screen	X
Human immunodeficiency virus, Hepatitis B and C screening	X
Molecular test for SARS-CoV-2[b]	

a. A full physical examination will include at a minimum, assessments of the skin, cardiovascular, respiratory, gastrointestinal, and neurological systems.

b. Two consecutive approved molecular tests (polymerase chain reaction or antigen test). The first test should be performed ≥7 days prior to admission.

Time and Events Table - Cohort 1

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7) Washout (Days 8-11)					Period 2 Treatment B (Days 12-21)		Period 3 Treatment A +Treatment B (Days 22-31)									Notes
	Day –2	Day –1	Day 1	Days 2-6	Day 7	Day 8-10	Day 11	Days 12-20	Day 21	Day 22	Day 23	Days 24-25	Day 26	Days 27-30	Day 31	Day 32	Days 33-34	Day 35	
Admit to clinic	X																		
Discharge from clinic																		X	
Brief physical examination	X				X		X		X				X					X	Includes, at a minimum, assessments of the skin, lungs, cardiovascular system, and abdomen (liver and spleen).
Vital sign measurements	X	X	X	D2	X		X	D12, D13, D17		X	X		X					X	Blood pressure and pulse measured in triplicate at pre-dose on Days 1, 12, and 22. Single blood pressure and pulse will be measured on other study days.
Temperature Check	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7) Washout (Days 8-11)					Period 2 Treatment B (Days 12-21)		Period 3 Treatment A +Treatment B (Days 22-31)									Notes
	Day –2	Day –1	Day 1	Days 2-6	Day 7	Day 8-10	Day 11	Days 12-20	Day 21	Day 22	Day 23	Days 24-25	Day 26	Days 27-30	Day 31	Day 32	Days 33-34	Day 35	
12-lead ECG	X		X		X		X	D12	X	X			X					X	ECGs on Days 1, 12, and 22, will be taken pre-dose, and at 2 and 4 and 6 hours post-dose. Pre-dose ECGs on Days 1, 12, and 22 will be taken in triplicate. The post-dose ECGs are single ECGs.
Drug, alcohol, and cotinine screen	X																		See Protocol Appendix 2 for tests.
Laboratory assessments (hematology, clinical chemistry, urinalysis)	X				X		X		X				X					X	See Protocol Appendix 2 for tests.

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7) Washout (Days 8-11)					Period 2 Treatment B (Days 12-21)		Period 3 Treatment A +Treatment B (Days 22-31)									Notes
	Day –2	Day –1	Day 1	Days 2-6	Day 7	Day 8-10	Day 11	Days 12-20	Day 21	Day 22	Day 23	Days 24-25	Day 26	Days 27-30	Day 31	Day 32	Days 33-34	Day 35	
Molecular test for SARS-CoV	X[1]			D6				D13, D20						D27				X	Test to be obtained every 7 days from Check-in (regardless of period or washout) while in-house. [1]The second test should be performed 24 hours prior to admission to the unit. Participants should be quarantined within the unit until the second test result is negative. Once the second test result is confirmed to be negative, they can be released into the unit and follow infection control practices.
Pregnancy test	X																	X	Urine pregnancy test to confirm status.
Columbia-Suicide	X						X			X					X				See Protocol Section 8.2.6 for

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7) Washout (Days 8-11)					Period 2 Treatment B (Days 12-21)		Period 3 Treatment A +Treatment B (Days 22-31)									Notes
	Day –2	Day –1	Day 1	Days 2-6	Day 7	Day 8-10	Day 11	Days 12-20	Day 21	Day 22	Day 23	Days 24-25	Day 26	Days 27-30	Day 31	Day 32	Days 33-34	Day 35	
Severity Rating Scale																			details.
Study intervention: DRV/RTV (BID)								X	X	X	X	X	X	X	X				See Protocol Section 6.1 for study intervention details.
Study intervention: GSK3640254 200 mg (QD)			X	X	X					X	X	X`	X	X	X				See Protocol Section 6.1 for study intervention details.
DRV/RTV PK sampling								D19, D20	X						X				Pre-dose Days 19, 20 and 21. Post Day 21 dose at 0.5, 1, 1.5, 2, 3, 4, 6, 8, and 12 hours post-dose. Pre-dose Day 31. Post Day 31 dose at 0.5, 1, 1.5, 2, 3, 4, 6, 8, and 12 hours.
GSK3640254 PK sampling				D5, D6	X	D8								D29, D30	X	X			Pre-dose Days 5, 6, and 7. Post Day 7 dose at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, and 24 hours. Pre-dose Days 29, 30, and 31.

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7) Washout (Days 8-11)					Period 2 Treatment B (Days 12-21)		Period 3 Treatment A +Treatment B (Days 22-31)									Notes
	Day –2	Day –1	Day 1	Days 2-6	Day 7	Day 8-10	Day 11	Days 12-20	Day 21	Day 22	Day 23	Days 24-25	Day 26	Days 27-30	Day 31	Day 32	Days 33-34	Day 35	
																			Post Day 31 dose at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, and 24 hours.
AE review			←==========→																
SAE review			←==========→																
Concomitant medication review			←==========→																

Abbreviations: AE = adverse event; BID = twice daily; D = day; DRV = darunavir; ECG = electrocardiogram; PK = pharmacokinetic; QD = once daily; RTV = ritonavir; SAE = serious adverse event.

Time and Events Table - Cohort 2

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7) Washout (Days 8-11)					Period 2 Treatment C (Days 12-21)		Period 3 Treatment A +Treatment C (Days 22-31)									Notes
	Day –2	Day -1	Day 1	Days 2-6	Day 7	Day 8-10	Day 11	Days 12-20	Day 21	Day 22	Day 23	Days 24-25	Day 26	Days 27-30	Day 31	Day 32	Days 33-35	Day 36	
Admit to clinic	X																		
Discharge from clinic																		X	

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7) Washout (Days 8-11)					Period 2 Treatment C (Days 12-21)		Period 3 Treatment A +Treatment C (Days 22-31)									Notes
	Day –2	Day -1	Day 1	Days 2-6	Day 7	Day 8-10	Day 11	Days 12-20	Day 21	Day 22	Day 23	Days 24-25	Day 26	Days 27-30	Day 31	Day 32	Days 33-35	Day 36	
Brief physical examination	X				X		X		X				X					X	Includes, at a minimum, assessments of the skin, lungs, cardiovascular system, and abdomen (liver and spleen).
Vital sign measurements	X	X	X	D2	X		X	D12, D13, D17		X	X		X					X	Blood pressure and pulse measured in triplicate at pre-dose on Days 1, 12, and 22. Single blood pressure and pulse will be measured on other study days.
Temperature Check	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7) Washout (Days 8-11)					Period 2 Treatment C (Days 12-21)		Period 3 Treatment A +Treatment C (Days 22-31)									Notes
	Day –2	Day -1	Day 1	Days 2-6	Day 7	Day 8-10	Day 11	Days 12-20	Day 21	Day 22	Day 23	Days 24-25	Day 26	Days 27-30	Day 31	Day 32	Days 33-35	Day 36	
12-lead ECG	X	X	X		X		X	D12	X	X			X					X	ECGs on Days 1, 12, and 22, will be taken pre--dose, and at 2, 4, and 6 hours post-dose. Pre-dose ECGs on Days 1, 12, and 22 will be taken in triplicate. The post-dose ECGs are single ECGs.
Drug, alcohol, and cotinine screen	X																		See Protocol Appendix 2 for tests.
Laboratory assessments (hematology, clinical chemistry, urinalysis)	X				X		X		X				X					X	See Protocol Appendix 2 for tests.

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7) Washout (Days 8-11)					Period 2 Treatment C (Days 12-21)		Period 3 Treatment A +Treatment C (Days 22-31)									Notes
	Day –2	Day -1	Day 1	Days 2-6	Day 7	Day 8-10	Day 11	Days 12-20	Day 21	Day 22	Day 23	Days 24-25	Day 26	Days 27-30	Day 31	Day 32	Days 33-35	Day 36	
Molecular test for SARS-CoV-2	X[1]			D6				D13, D20						D27				X	Test to be obtained every 7 days from Check-in (regardless of period or washout) while in-house. [1]The second test should be performed 24 hours prior to admission to the unit. Participants should be quarantined within the unit until the second test result is negative. Once the second test result is confirmed to be negative, they can be released into the unit and follow infection control practices.
Pregnancy test	X																	X	Urine pregnancy test to confirm status.
Columbia-Suicide Severity Rating Scale	X						X			X					X				See Protocol Section 8.2.6 for details.
Study intervention: ETR (BID)								X	X	X	X	X	X	X	X				See Protocol Section 6.1 for study intervention details.

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7) Washout (Days 8-11)					Period 2 Treatment C (Days 12-21)		Period 3 Treatment A +Treatment C (Days 22-31)									Notes
	Day –2	Day -1	Day 1	Days 2-6	Day 7	Day 8-10	Day 11	Days 12-20	Day 21	Day 22	Day 23	Days 24-25	Day 26	Days 27-30	Day 31	Day 32	Days 33-35	Day 36	
Study intervention: GSK3640254 200 mg (QD)			X	X	X					X	X	X`	X	X	X				See Protocol Section 6.1 for study intervention details.
ETR PK sampling								D19, D20	X						X				Pre-dose Days 19, 20 and 21. Post Day 21 dose at 0.5, 1, 1.5, 2, 3, 4, 6, 8, and 12 hours post-dose. Pre-dose Day 31. Post Day 31 dose at 0.5, 1, 1.5, 2, 3, 4, 6, 8, and 12 hours.
GSK3640254 PK sampling				D5, D6	X	D8								D29, D30	X	X			Pre-dose Days 5, 6, and 7. Post Day 7 dose at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, and 24 hours. Pre-dose Days 29, 30, and 31. Post Day 31 dose at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, and 24 hours.
AE review			←==========															→	
SAE review		←==========																→	

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7) Washout (Days 8-11)					Period 2 Treatment C (Days 12-21)		Period 3 Treatment A +Treatment C (Days 22-31)								Notes
	Day –2	Day -1	Day 1	Days 2-6	Day 7	Day 8-10	Day 11	Days 12-20	Day 21	Day 22	Day 23	Days 24-25	Day 26	Days 27-30	Day 31	Day 32	Days 33-35	Day 36	
Concomitant medication review		←==========→																	

Abbreviations: AE = adverse event; BID = twice daily; D = day; ECG = electrocardiogram; ETR = etravirine; PK = pharmacokinetic; QD = once daily; SAE = serious adverse event.

Time and Events Table - Cohort 3

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7)			Period 2 Treatment A + Treatment B + Treatment C (Days 8-21)												Notes
	Day –2	Day -1	Day 1	Days 2-6	Day 7	Day 8	Day 9	Days 10-12	Day 13	Day 14	Days 15-16	Day 17	Days 18-20	Day 21	Day 22	Days 23-25	Day 26	
Admit to clinic	X																	
Discharge from clinic																	X	
Brief physical examination	X				X					X							X	Includes, at a minimum, assessments of the skin, lungs, cardiovascular system, and abdomen (liver and spleen).
Vital sign measurements	X	X	X	D2	X	X				X		X					X	Blood pressure and pulse measured in triplicate at pre-dose on Days 1 and 8. Single blood pressure and pulse will be measured on other study days.
Temperature Check	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
12-lead ECG	X	X	X			X	X										X	ECGs on Days 1, 8, and 9 will be taken pre-dose, and at 2, 4, and 6 hours post-dose. Pre-dose ECGs on Days 1, 8, and 9 will be taken in triplicate. The post-dose ECGs are single ECGs.
Drug, alcohol, and cotinine screen	X																	See Protocol Appendix 2 for tests.

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7)			Period 2 Treatment A + Treatment B + Treatment C (Days 8-21)											Notes
	Day –2	Day -1	Day 1	Days 2-6	Day 7	Day 8	Day 9	Days 10-12	Day 13	Day 14	Days 15-16	Day 17	Days 18-20	Day 21	Day 22	Days 23-25	Day 26	
Laboratory assessments (hematology, clinical chemistry, urinalysis)	X				X					X							X	See Protocol Appendix 2 for tests.
Molecular Test for SARS-CoV-2	X[1]			D6					X				D20				X	Test to be obtained every 7 days from Check-in (regardless of period or washout) while in-house.[1] The second test should be performed 24 hours prior to admission to the unit. Participants should be quarantined within the unit until the second test result is negative. Once the second test result is confirmed to be negative, they can be released into the unit and follow infection control practices.
Pregnancy test	X																X	Urine pregnancy test to confirm status.
Columbia-Suicide Severity Rating Scale	X					X			X					X				See Protocol Section 8.2.6 for details.
Study intervention: DRV/RTV and ETR (BID)						X	X	X	X	X	X	X	X	X				See Protocol Section 6.1 for study intervention details.

Procedure	Check-in	Baseline	Period 1 Treatment A (Days 1-7)			Period 2 Treatment A + Treatment B + Treatment C (Days 8-21)											Notes
	Day –2	Day -1	Day 1	Days 2-6	Day 7	Day 8	Day 9	Days 10-12	Day 13	Day 14	Days 15-16	Day 17	Days 18-20	Day 21	Day 22	Days 23-25	Day 26	
Study intervention: GSK3640254 200 mg (QD)			X	X	X	X	X	X	X	X	X`	X	X	X				See Protocol Section 6.1 for study intervention details.
DRV/RTV and ETR PK sampling													D19, D20	X				Pre-dose Days 19, 20, and 21. Post Day 21 dose at 0.5, 1, 1.5, 2, 3, 4, 6, 8, and 12 hours.
GSK3640254 PK sampling				D5, D6	X	X								X	X			Pre-dose Days 5, 6, and 7. Post Day 7 dose at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, and 24 hours. Pre-dose Day 21. Post Day 21 dose at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, and 24 hours.
AE review			←==========→															
SAE review		←==========→																
Concomitant medication review		←==========→																

AE = adverse event; BID = twice daily; D = day; DRV = darunavir; ECG = electrocardiogram; ETR = etravirine; PK = pharmacokinetic; QD = once daily; RTV = ritonavir; SAE = serious adverse event.

- Participants will fast overnight for at least 8 hours prior to breakfast and before the AM dose and for at least 2 hours prior to dinner and before the PM dose. Participants will receive the moderate fat meal 30 minutes prior to dosing. Participants will eat this meal in 25 minutes or less. Dose administration will occur within 5 minutes of completion of meal consumption.

- Serial PK blood samples will be collected before (at 0 hour) and after the AM study drug administration at the time points listed. For the study interventions that are administered twice daily (BID) (DRV/RTV and ETR), the 12-hour sample will be collected before the PM dose.
- Day 35 for Cohort 1, Day 36 for Cohort 2, and Day 26 for Cohort 3 is study discharge. Evaluations scheduled for study discharge will also be performed for participants who discontinue prior to completing.
- The timing of planned study assessments may change during the course of the study based on emerging data/in-stream data review (e.g., to obtain data closer to the time of peak plasma concentrations) to ensure appropriate monitoring.

Any changes in the timing of time points for any planned study assessments as the result of emerging PK data from this study must be documented and approved by the relevant study team member and then archived in the sponsor and site study files but will not constitute a protocol amendment. The Institutional Review Board/ Independent Ethics Committee will be informed of any safety issues that constitute a substantial amendment and require alteration of the safety monitoring scheme or amendment of the informed consent form. The changes will be approved by the health authority and the ethics committee before implementation

10.2. Appendix 2: Study Phases and Treatment Emergent Adverse Events

10.2.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to study treatment start date(/time) and stop date(/time).

10.2.1.1. Study Phases for Lab, Electrocardiograms, and Vital Signs

Assessments and events will be classified according to the time of occurrence relative to study treatment start date(/time) and stop date(/time).

Study Phase	Definition
Pre-Treatment	Date and Time ≤Study Treatment Start Date and Time
On-Treatment	Study Treatment Start Date and Time <Date and Time ≤Study Treatment Stop Date and Time + 5 days
Post-Treatment	Date and Time >Study Treatment Stop Date and Time + 5 days

10.2.1.2. Study Phases for Concomitant Medication

Study Phase	Study Phase
Prior	Prior
Concomitant	Concomitant

NOTES:
Please refer to Appendix 5: Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

10.2.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• If AE onset date and time is on or after treatment start date and time & on or before treatment stop date and time + 5 days. • Study Treatment Start Date and Time ≤AE Start Date and Time ≤Study Treatment Stop Date and Time + 5 days. • If the AE onset date is completely missing, the AE is considered as treatment emergent.

NOTES:
- If the study treatment stop date is missing, then the AE will be considered to be On-Treatment.
- Please refer to Appendix 5: Reporting Standards for Missing Data for handling of missing and partial dates for AEs. Use the rules in this table if the AE onset date is completely missing.

10.3. Appendix 3: Data Display Standards & Handling Conventions

10.3.1. Reporting Process

Software	
• The currently supported versions of SAS software (9.4) will be used.	
Reporting Area	
HARP Server	\\us1salx00259.corpnet2.com
HARP Compound	\gsk3640254\mid213054\final_01
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1). • For creation of ADaM datasets (ADC1/ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM.	
Generation of RTF Files	
• RTF files will be generated for all reporting efforts described in the RAP.	

10.3.2. Reporting Standards

General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: PPD :
  • 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
• Do not include participant level listings in the main body of the GSK Clinical Study Report. All participant level listings should be located in the modular appendices as ICH or non-ICH listings.

Formats
• All data will be reported according to the actual treatment the participant received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be rounded to integer, unless otherwise specified. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical 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 IDSL Statistical Principle 5.05.1).

• Unscheduled or unplanned readings will be presented within the participant's listings. • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures (mean figures only for PK concentrations), summaries, and statistical analyses (excluding statistical analyses of PK parameters).
Unscheduled Visits
• Unscheduled visits will not be included in summary tables except for determining the worst-case values. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.
Descriptive Summary Statistics
Continuous Data: Refer to IDSL Statistical Principle 6.06.1
Categorical Data: N, n, frequency, %
Graphical Displays
• Refer to IDSL Statistical Principals 7.01 to 7.13.

10.3.3. Reporting Standards for Pharmacokinetics

Pharmacokinetic Concentration Data	

Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards.
	Refer to IDSL Statistical Principle 6.06.1.
	For continuous data:
	• NQs at the beginning of a participant profile (i.e. before the first incidence of a measurable concentration) are deemed to be zero as it is assumed that in this circumstance no drug is yet measurable in the blood.
	• For NQs at the end of the participant profile (i.e. after the last incidence of a measurable concentration);
	  • for individual plots and PK analyses these are dropped (set to missing) as they do not provide any useful information (and can erroneously indicate that absolutely no drug is present)
	  • for summary statistics, these are set to 0 (to avoid skewing of the summary statistics)
	• Individual NQs which fall between two measurable concentrations are set to missing (individual values of this nature are assumed to be an anomaly)
	If two or more NQ values occur in succession between measurable concentrations, the profile will be deemed to have terminated at the last measurable concentration prior to these NQs. For the purpose of individual participant plots, these NQs will be set to 0, and the subsequent measurable concentrations will be retained. For the derivation of pharmacokinetic parameters, these NQs and any subsequent measurable concentrations will be omitted (set to missing).
	Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.

Pharmacokinetic Parameter Data	
Descriptive Summary Statistics, Graphical Displays and Listings	N, n, arithmetic mean, 95% CI of arithmetic mean, geometric mean, 95% CI of geometric mean, SD, SD of log (ln) data, CV (%), and between-subject geometric coefficient of variation (CVb (%)) will be reported. CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD[ln] = SD of Ln-Transformed data)

Parameters Not Being Ln-Transformed	Tmax, λz, λz lower, λz upper, and λz no. of points.
Parameters Not Being Summarized	λz, λz lower, λz upper, and λz no. of points.
Listings	Include the first point, last point and number of points used in the determination of λz and Rsq_adjusted for listings.

10.4. Appendix 4: Derived and Transformed Data

10.4.1. 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. • The worst finding/interpretation associated with multiple measurements as the finding/interpretation for that time point. • 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 Dose Date on Day 1:
  • Assessment Date = Missing
  → Study Day = Missing
  • Assessment Date <Dose Date on Day 1
  → Study Day = Assessment Date –Dose Date on Day 1
  • Assessment Date >= Dose Date on Day 1
  → Study Day = Assessment Date – Dose Date on Day 1 + 1

10.4.2. Study Population

Age

• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  o Any participant with a missing day will have this imputed as day '15'.
  o Any participant with a missing day and month will have this imputed as '30th June'.
• Birth date will be presented in listings as 'YYYY'.

Body Mass Index (BMI)
• Calculated as Weight (kg) / [Height $(m)^2$]

10.4.3. Safety

Adverse Events
AEs of Special Interest
• QT prolongation • Gastrointestinal intolerability and gastric toxicity • Psychiatric events • Nervous system disorders • Skin and subcutaneous tissue disorders

12-Lead Electrocardiograms
QTcB Interval
• QTcB interval in msec will be calculated using QT interval (msec) and RR interval (msec) as $QTcB = \frac{QT}{\sqrt{\frac{RR}{1000}}}$ where RR interval in msec is calculated using QT interval (msec) and QTcF interval (msec) as $RR = (\frac{QT}{QTcF})^3 \times 1000$

10.5. Appendix 5: Reporting Standards for Missing Data

10.5.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (i.e., as specified in the protocol) is defined as the participant has completed all phases of the study including the final date on which data were or are expected to be collected. • Withdrawn participants will not be replaced in the study. • All available data from participants who are withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

10.5.2. 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: ○ 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. ○ 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.

10.5.2.1. Handling of Missing and Partial Dates

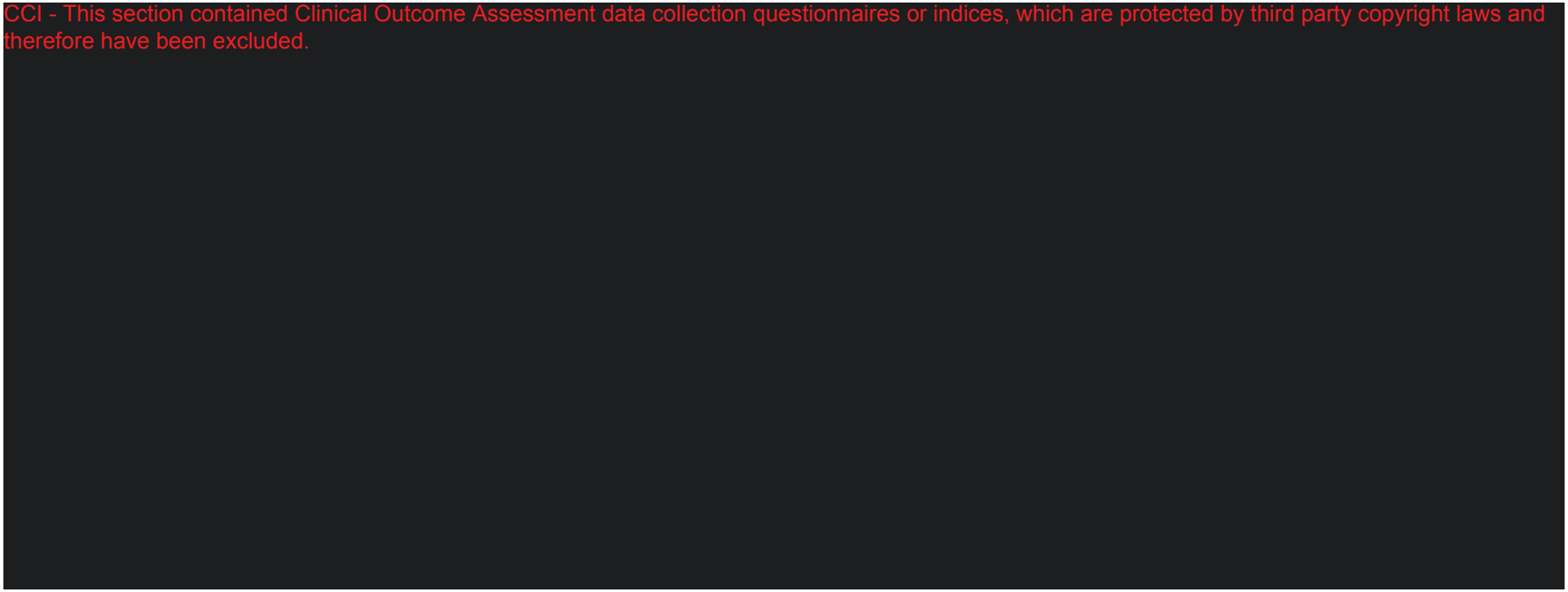
Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: ○ Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Section 10.2.2. ○ Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.
Concomitant Medications	• Partial dates for any concomitant medications recorded in the eCRF will be imputed using the following convention: • If the partial date is a start date, a "01" will be used for the day and "Jan" will be used for the month • If the partial date is a stop date, a "28/29/30/31" will be used for the day (dependent on the month and year) and "Dec" will be used for the month. • The recorded partial date will be displayed in listings.

10.6. Appendix 6: Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events

10.6.1. Laboratory Values

Laboratory abnormalities will be graded according to the DAIDS grading table Version 2.1, July 2017. Laboratory results are converted to use SI units; only the numeric part of the criteria will be used. If for a laboratory parameter there are multiple grades sharing the same criteria, the maximum grade will be used.

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.



CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.

10.7. Appendix 7: Values of Potential Clinical Importance

10.7.1. ECG

ECG Parameter	Units	Potential Clinically Important Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec		>450
Absolute PR Interval	msec	<110	>200
Absolute QRS Interval	msec	<75	>110
Change from Baseline			
Increase from Baseline QTc	msec		>60

10.7.2. Vital Signs

Vital Sign Parameter (Absolute)	Units	Potential Clinically Important Range	
		Lower	Upper
Systolic Blood Pressure	mmHg	<85	>140
Diastolic Blood Pressure	mmHg	<45	>90
Heart Rate	Beats per minute	<40	>100

10.8. Appendix 8: Abbreviations & Trademarks

10.8.1. Abbreviations

Abbreviation	Description
ADaM	analysis data model
AE	adverse event
ALT	alanine aminotransferase
AUC	area under the plasma concentration-time curve
AUC(0-τ)	AUC from time 0 to the end of the dosing interval at steady state
BID	twice daily
CDISC	Clinical Data Interchange Standards Consortium
CI	confidence interval
Cmax	maximum observed concentration
CSR	clinical study report
C-SSRS	Columbia suicide severity rating scale
Cτ	plasma concentration at the end of the dosing interval
CV_b	coefficient of variation (between)
CVw	coefficient of variability (within)
DAIDS	division of AIDS
DBF	database freeze
DBR	database release
DP	decimal places
DRV	darunavir
ECG	electrocardiogram
eCRF	electronic case record form
GSK	GlaxoSmithKline
ETR	etravirine
HIV	human immunodeficiency virus
ICH	international conference on harmonization
IDSL	integrated data standards library
LLN	lower limit of normal
NQ	not quantifiable
PK	pharmacokinetic
QD	once daily
RAP	reporting & analysis plan
SAC	statistical analysis complete
SAE	serious adverse event
SD	standard deviation
SDTM	study data tabulation model
SMQ	Standardized MedDRA Query
Tmax	time of maximum observed concentration
ULN	upper limit of normal

10.8.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
WinNonlin

10.9. Appendix 9: List of Data Displays

10.9.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.8	
Safety	2.1 to 2.30	2.1 to 2.1
Pharmacokinetic	3.1 to 3.42	3.1 to 3.45
Section	**Listings**	
ICH Listings	1 to 32	
Non-ICH Listings	33 to 43	

10.9.2. Mock Example Shell Referencing

Non-IDSL specifications will be referenced as indicated and if required example mock-up displays provided in the Table/Listing/Figure Shells.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln

NOTES:

- Non-Standard displays are indicated in the 'IDSL / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

10.9.3. Deliverables

Delivery	Description
SAC	Final Statistical Analysis Complete

10.9.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Enrolled	NS1	Summary of Number of Subjects Enrolled by Country and Site ID		SAC
1.2.	Screened	SP1	Summary of Study Population		SAC
1.3.	Safety	ES1	Summary of Subject Disposition for the Subject Conclusion Record		SAC
1.4.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failures		SAC
Protocol Deviation					
1.5.	Safety	DV1	Summary of Important Protocol Deviations		SAC
Demographic and Baseline Characteristics					
1.6.	Safety	DM1	Summary of Demographic Characteristics		SAC
1.7.	Safety	DM5	Summary of Race and Racial Combinations		SAC
1.8.	Safety	DM11	Summary of Age Ranges		SAC

10.9.5. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
2.1.	Safety	AE1CP	Summary of Adverse Events by System Organ Class and Preferred Term		SAC
2.2.	Safety	AE1CP	Summary of Drug-Related Adverse Events by System Organ Class and Preferred Term		SAC
2.3.	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency		SAC
2.4.	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC
2.5.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC
2.6.	Safety	AE5A	Summary of Adverse Events by System Organ Class and Preferred Term and Maximum Intensity		SAC
2.7.	Safety	AE1CP	Summary of Adverse Events of Special Interest		SAC
Laboratory: Chemistry					
2.8.	Safety	LB1	Summary of Clinical Chemistry Changes from Baseline		SAC
2.9.	Safety	LB1	Summary of Clinical Chemistry Values		SAC
2.10.	Safety	LB16	Summary of Clinical Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline		SAC
Laboratory: Hematology					

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.11.	Safety	LB1	Summary of Hematology Changes from Baseline		SAC
2.12.	Safety	LB1	Summary of Hematology Values		SAC
2.13.	Safety	LB16	Summary of Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline		SAC
Laboratory: Urinalysis					
2.14.	Safety	UR3	Summary of Urinalysis Dipstick Results		SAC
2.15.	Safety	LB1	Summary of Urine Concentration Changes from Baseline		SAC
2.16.	Safety	LB1	Summary of Urine Concentration Values		SAC
2.17.	Safety	LB16	Summary of Urinalysis by Maximum Grade Increase Post-Baseline Relative to Baseline		SAC
ECG					
2.18.	Safety	SAFE_T1	Summary of ECG Findings		SAC
2.19.	Safety	EG2	Summary of ECG Changes from Baseline		SAC
2.20.	Safety	EG2	Summary of ECG Values		SAC
2.21.	Safety	EG10	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category		SAC
2.22.	Safety	EG11	Summary of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category		SAC
Vital Signs					
2.23.	Safety	VS1	Summary of Vital Sign Changes from Baseline		SAC
2.24.	Safety	VS1	Summary of Vital Sign Values		SAC
C-SSRS					

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.25.	Safety	CSSRS4	Listing of C-SSRS Suicidal Ideation and Behaviour Data	Only include participants who have suicidal ideation or behaviour	SAC
Liver Event					
2.26.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting		SAC
2.27.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities		SAC
COVID-19 Related AE					
2.28.	Safety	PAN1	Summary of COVID-19 Assessment		SAC
2.29	Safety	SAFE_T2	Summary of COVID-19 Adverse Event		SAC
2.30	Safety	PAN11	Summary of COVID-19 Symptoms for Subjects with Adverse Events	Conditional Display	SAC

10.9.6. Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ECG					
2.1.	Safety	EG9	Mean (95% CI) Change from Baseline in QTcF Interval by Timepoint and Treatment		SAC

10.9.7. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
PK Concentration Data					
3.1.	PK Concentration	PKCT1	Summary of GSK3640254 Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment – Cohort 1		SAC
3.2.	PK Concentration	PKCT1	Summary of Darunavir Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment – Cohort 1		SAC
3.3.	PK Concentration	PKCT1	Summary of Ritonavir Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment – Cohort 1		SAC
3.4.	PK Concentration	PKCT1	Summary of Predose (trough) GSK3640254 Plasma Concentration Data (units) by Treatment – Cohort 1		SAC
3.5.	PK Concentration	PKCT1	Summary of Predose (trough) Darunavir Plasma Concentration Data (units) by Treatment – Cohort 1		SAC
3.6.	PK Concentration	PKCT1	Summary of Predose (trough) Ritonavir Plasma Concentration Data (units) by Treatment – Cohort 1		SAC
3.7.	PK Concentration	PKCT1	Summary of GSK3640254 Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment – Cohort 2		SAC
3.8.	PK Concentration	PKCT1	Summary of Etravirine Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment – Cohort 2		SAC
3.9.	PK Concentration	PKCT1	Summary of Predose (trough) GSK3640254 Plasma Concentration Data (units) by Treatment – Cohort 2		SAC
3.10.	PK Concentration	PKCT1	Summary of Predose (trough) Etravirine Plasma Concentration Data (units) by Treatment – Cohort 2		SAC
3.11.	PK Concentration	PKCT1	Summary of GSK3640254 Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment – Cohort 3		SAC

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.12.	PK Concentration	PKCT1	Summary of Darunavir Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment – Cohort 3		SAC
3.13.	PK Concentration	PKCT1	Summary of Ritonavir Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment – Cohort 3		SAC
3.14.	PK Concentration	PKCT1	Summary of Etravirine Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment – Cohort 3		SAC
3.15.	PK Concentration	PKCT1	Summary of Predose (trough) GSK3640254 Plasma Concentration Data (units) by Treatment – Cohort 3		SAC
3.16.	PK Concentration	PKCT1	Summary of Predose (trough) Darunavir Plasma Concentration Data (units) by Treatment – Cohort 3		SAC
3.17.	PK Concentration	PKCT1	Summary of Predose (trough) Ritonavir Plasma Concentration Data (units) by Treatment – Cohort 3		SAC
3.18.	PK Concentration	PKCT1	Summary of Predose (trough) Etravirine Plasma Concentration Data (units) by Treatment – Cohort 3		SAC
PK Derived Parameters					
3.19.	PK Parameter	PKPT4	Summary Statistics of Derived GSK3640254 Plasma Pharmacokinetic Parameters (Non-Transformed) Based on Actual Time by Treatment – Cohort 1		SAC
3.20.	PK Parameter	PKPT4	Summary Statistics of Derived GSK3640254 Plasma Pharmacokinetic Parameters (Ln-Transformed) Based on Actual Time by Treatment – Cohort 1		SAC
3.21.	PK Parameter	PKPT4	Summary Statistics of Derived Darunavir Plasma Pharmacokinetic Parameters (Non-Transformed) Based on Actual Time by Treatment – Cohort 1		SAC

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.22.	PK Parameter	PKPT4	Summary Statistics of Derived Darunavir Plasma Pharmacokinetic Parameters (Ln-Transformed) Based on Actual Time by Treatment – Cohort 1		SAC
3.23.	PK Parameter	PKPT4	Summary Statistics of Derived Ritonavir Plasma Pharmacokinetic Parameters (Non-Transformed) Based on Actual Time by Treatment – Cohort 1		SAC
3.24.	PK Parameter	PKPT4	Summary Statistics of Derived Ritonavir Plasma Pharmacokinetic Parameters (Ln-Transformed) Based on Actual Time by Treatment – Cohort 1		SAC
3.25.	PK Parameter	PKPT4	Summary Statistics of Derived GSK3640254 Plasma Pharmacokinetic Parameters (Non-Transformed) Based on Actual Time by Treatment – Cohort 2		SAC
3.26.	PK Parameter	PKPT4	Summary Statistics of Derived GSK3640254 Plasma Pharmacokinetic Parameters (Ln-Transformed) Based on Actual Time by Treatment – Cohort 2		SAC
3.27.	PK Parameter	PKPT4	Summary Statistics of Derived Etravirine Plasma Pharmacokinetic Parameters (Non-Transformed) Based on Actual Time by Treatment – Cohort 2		SAC
3.28.	PK Parameter	PKPT4	Summary Statistics of Derived Etravirine Plasma Pharmacokinetic Parameters (Ln-Transformed) Based on Actual Time by Treatment – Cohort 2		SAC
3.29.	PK Parameter	PKPT4	Summary Statistics of Derived GSK3640254 Plasma Pharmacokinetic Parameters (Non-Transformed) Based on Actual Time by Treatment – Cohort 3		SAC
3.30.	PK Parameter	PKPT4	Summary Statistics of Derived GSK3640254 Plasma Pharmacokinetic Parameters (Ln-Transformed) Based on Actual Time by Treatment – Cohort 3		SAC

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.31.	PK Parameter	PKPT4	Summary Statistics of Derived Darunavir Plasma Pharmacokinetic Parameters (Non-Transformed) Based on Actual Time by Treatment – Cohort 3		SAC
3.32.	PK Parameter	PKPT4	Summary Statistics of Derived Darunavir Plasma Pharmacokinetic Parameters (Ln-Transformed) Based on Actual Time by Treatment – Cohort 3		SAC
3.33.	PK Parameter	PKPT4	Summary Statistics of Derived Ritonavir Plasma Pharmacokinetic Parameters (Non-Transformed) Based on Actual Time by Treatment – Cohort 3		SAC
3.34.	PK Parameter	PKPT4	Summary Statistics of Derived Ritonavir Plasma Pharmacokinetic Parameters (Ln-Transformed) Based on Actual Time by Treatment – Cohort 3		SAC
3.35.	PK Parameter	PKPT4	Summary Statistics of Derived Etravirine Plasma Pharmacokinetic Parameters (Non-Transformed) Based on Actual Time by Treatment – Cohort 3		SAC
3.36.	PK Parameter	PKPT4	Summary Statistics of Derived Etravirine Plasma Pharmacokinetic Parameters (Ln-Transformed) Based on Actual Time by Treatment – Cohort 3		SAC
PK Analysis Tables					
3.37.	PK Parameter	PKPT3	Statistical Analysis of GSK3640254 Plasma Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Cohort 1	AUC(0-tau) and Cmax	SAC
3.38.	PK Parameter	PKPT3	Statistical Analysis of Darunavir Plasma Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Cohort 1	AUC(0-tau) and Cmax	SAC
3.39.	PK Parameter	PKPT3	Statistical Analysis of Ritonavir Plasma Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Cohort 1	AUC(0-tau) and Cmax	SAC

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
3.40.	PK Parameter	PKPT3	Statistical Analysis of GSK3640254 Plasma Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Cohort 2	AUC(0-tau) and Cmax	SAC
3.41.	PK Parameter	PKPT3	Statistical Analysis of Etravirine Plasma Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Cohort 2	AUC(0-tau) and Cmax	SAC
3.42.	PK Parameter	PKPT3	Statistical Analysis of GSK3640254 Plasma Pharmacokinetic Parameters: Analysis of Variance (ANOVA) – Cohort 3	AUC(0-tau) and Cmax	SAC

10.9.8. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Individual Concentration Plots					
3.1.	PK Concentration	PKCF1	Individual GSK3640254 Plasma Concentration-Time Plots by Participant – Cohort 1 (Linear and Semi-Logarithmic)	Paginate by Participant Dashed line represents the LLQ Treatments Overlaid	SAC
3.2.	PK Concentration	PKCF1	Individual Darunavir Plasma Concentration-Time Plots by Participant – Cohort 1 (Linear and Semi-Logarithmic)	Paginate by Participant Dashed line represents the LLQ Treatments Overlaid	SAC
3.3.	PK Concentration	PKCF1	Individual Ritonavir Plasma Concentration-Time Plots by Participant – Cohort 1 (Linear and Semi-Logarithmic)	Paginate by Participant Dashed line represents the LLQ Treatments Overlaid	SAC
3.4.	PK Concentration	PKCF1	Individual GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)	Paginate by Treatment Dashed line represents the LLQ Participants Overlaid	SAC
3.5.	PK Concentration	PKCF1	Individual Darunavir Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)	Paginate by Treatment Dashed line represents the LLQ Participants Overlaid	SAC
3.6.	PK Concentration	PKCF1	Individual Ritonavir Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)	Paginate by Treatment Dashed line represents the LLQ Participants Overlaid	SAC
3.7.	PK Concentration	PKCF1	Individual GSK3640254 Plasma Concentration-Time Plots by Participant – Cohort 2 (Linear and Semi-Logarithmic)	Paginate by Participant Dashed line represents the LLQ Treatments Overlaid	SAC

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.8.	PK Concentration	PKCF1	Individual Etravirine Plasma Concentration-Time Plots by Participant – Cohort 2 (Linear and Semi-Logarithmic)	Paginate by Participant Dashed line represents the LLQ Treatments Overlaid	SAC
3.9.	PK Concentration	PKCF1	Individual GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 2 (Linear and Semi-Logarithmic)	Paginate by Treatment Dashed line represents the LLQ Participants Overlaid	SAC
3.10.	PK Concentration	PKCF1	Individual Etravirine Plasma Concentration-Time Plots by Treatment – Cohort 2 (Linear and Semi-Logarithmic)	Paginate by Treatment Dashed line represents the LLQ Participants Overlaid	SAC
3.11.	PK Concentration	PKCF1	Individual GSK3640254 Plasma Concentration-Time Plots by Participant – Cohort 3 (Linear and Semi-Logarithmic)	Paginate by Participant Dashed line represents the LLQ Treatments Overlaid	SAC
3.12.	PK Concentration	PKCF1	Individual Darunavir Plasma Concentration-Time Plots by Participant – Cohort 3 (Linear and Semi-Logarithmic)	Paginate by Participant Dashed line represents the LLQ	SAC
3.13.	PK Concentration	PKCF1	Individual Ritonavir Plasma Concentration-Time Plots by Participant – Cohort 3 (Linear and Semi-Logarithmic)	Paginate by Participant Dashed line represents the LLQ	SAC
3.14.	PK Concentration	PKCF1	Individual Etravirine Plasma Concentration-Time Plots by Participant – Cohort 3 (Linear and Semi-Logarithmic)	Paginate by Participant Dashed line represents the LLQ	SAC
3.15.	PK Concentration	PKCF1	Individual GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)	Paginate by Treatment Dashed line represents the LLQ Participants Overlaid	SAC
3.16.	PK Concentration	PKCF1	Individual Darunavir Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)	Dashed line represents the LLQ Participants Overlaid	SAC

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.17.	PK Concentration	PKCF1	Individual Ritonavir Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)	Dashed line represents the LLQ Participants Overlaid	SAC
3.18.	PK Concentration	PKCF1	Individual Etravirine Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)	Dashed line represents the LLQ Participants Overlaid	SAC
Mean / Median Concentration Plots					
3.19.	PK Concentration	PKCF2	Mean (Standard Deviation) GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.20.	PK Concentration	PKCF2	Mean (Standard Deviation) Darunavir Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.21.	PK Concentration	PKCF2	Mean (Standard Deviation) Ritonavir Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.22.	PK Concentration	PKCF3	Median (Range) GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.23.	PK Concentration	PKCF3	Median (Range) Darunavir Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.24.	PK Concentration	PKCF3	Median (Range) Ritonavir Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.25.	PK Concentration	PKCF2	Mean (Standard Deviation) Predose (Trough) GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)		SAC
3.26.	PK Concentration	PKCF2	Mean (Standard Deviation) Predose (Trough) Darunavir Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)		SAC

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.27.	PK Concentration	PKCF2	Mean (Standard Deviation) Predose (Trough) Ritonavir Plasma Concentration-Time Plots by Treatment – Cohort 1 (Linear and Semi-Logarithmic)		SAC
3.28.	PK Concentration	PKCF2	Mean (Standard Deviation) GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 2 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.29.	PK Concentration	PKCF2	Mean (Standard Deviation) Etravirine Plasma Concentration-Time Plots by Treatment – Cohort 2 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.30.	PK Concentration	PKCF3	Median (Range) GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 2 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.31.	PK Concentration	PKCF3	Median (Range) Etravirine Plasma Concentration-Time Plots by Treatment – Cohort 2 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.32.	PK Concentration	PKCF2	Mean (Standard Deviation) Predose (Trough) GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 2 (Linear and Semi-Logarithmic)		SAC
3.33.	PK Concentration	PKCF2	Mean (Standard Deviation) Predose (Trough) Etravirine Plasma Concentration-Time Plots by Treatment – Cohort 2 (Linear and Semi-Logarithmic)		SAC
3.34.	PK Concentration	PKCF2	Mean (Standard Deviation) GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.35.	PK Concentration	PKCF2	Mean (Standard Deviation) Darunavir Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)		SAC

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.36.	PK Concentration	PKCF2	Mean (Standard Deviation) Ritonavir Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)		SAC
3.37.	PK Concentration	PKCF2	Mean (Standard Deviation) Etravirine Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)		SAC
3.38.	PK Concentration	PKCF3	Median (Range) GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)	Treatments Overlaid	SAC
3.39.	PK Concentration	PKCF3	Median (Range) Darunavir Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)		SAC
3.40.	PK Concentration	PKCF3	Median (Range) Ritonavir Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)		SAC
3.41.	PK Concentration	PKCF3	Median (Range) Etravirine Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)		SAC
3.42.	PK Concentration	PKCF2	Mean (Standard Deviation) Predose (Trough) GSK3640254 Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)		SAC
3.43.	PK Concentration	PKCF2	Mean (Standard Deviation) Predose (Trough) Darunavir Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)		SAC
3.44.	PK Concentration	PKCF2	Mean (Standard Deviation) Predose (Trough) Ritonavir Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)		SAC
3.45.	PK Concentration	PKCF2	Mean (Standard Deviation) Predose (Trough) Etravirine Plasma Concentration-Time Plots by Treatment – Cohort 3 (Linear and Semi-Logarithmic)		SAC

10.9.9. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Safety	ES3	Listing of Reasons for Study Withdrawal		SAC
2.	Safety	SD2	Listing of Reasons for Study Treatment Discontinuation		SAC
3.	Screened	ES7	Listing of Reasons for Screen Failure		SAC
Protocol Deviations					
4.	Safety	DV2	Listing of Important Protocol Deviations		SAC
5.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC
Populations Analyzed					
6.	Safety	SP3A	Listing of Subjects Excluded from Any Population		SAC
Demographic and Baseline Characteristics					
7.	Safety	DM2	Listing of Demographic Characteristics		SAC
8.	Safety	DM9	Listing of Race		SAC
Prior and Concomitant Medications					
9.	Safety	CM5	Listing of Concomitant Medications	Based on GSK Drug Dictionary	SAC
Exposure and Treatment Compliance					
10.	Safety	EX4	Listing of Exposure Data		SAC
11.	Safety	POP_L1	Listing of Meal Data		SAC
Adverse Events					
12.	Safety	AE2	Listing of Relationship Between System Organ Class and Verbatim Text		SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
13.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events		SAC
14.	Safety	AE9CP	Listing of All Adverse Events		SAC
15.	Safety	AE9CP	Listing of Adverse Events of Special Interest		SAC
Serious and Other Significant Adverse Events					
16.	Safety	AE9CP	Listing of Study Drug Related Adverse Events		SAC
17.	Safety	AE9CP	Listing of Serious Adverse Events (Fatal & Non-Fatal)		SAC
18.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event		SAC
19.	Safety	AE9CP	Listing of Adverse Events Leading to Withdrawal from Study		SAC
Hepatobiliary (Liver)					
20.	Safety	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events		SAC
21.	Safety	SU2	Listing of Substance Use for Subjects with Liver Stopping Events		SAC
All Laboratory					
22.	Safety	LB5A	Listing of Clinical Chemistry with any Toxicities		SAC
23.	Safety	LB5A	Listing of All Clinical Chemistry Data for Subjects with any Toxicities		SAC
24.	Safety	LB5A	Listing of Hematology with any Toxicities		SAC
25.	Safety	LB5A	Listing of All Hematology Data for Subjects with any Toxicities		SAC
26.	Safety	LB5A	Listing of Urinalysis with any Toxicities		SAC
27.	Safety	LB5A	Listing of All Urinalysis Data for Subjects with any Toxicities		SAC
ECG					
28.	Safety	EG6	Listing of All ECG Findings		SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
29.	Safety	EG6	Listing of All Abnormal ECG Findings		SAC
30.	Safety	EG4	Listing of All ECG Values		SAC
Vital Signs					
31.	Safety	VS5	Listing of All Vital Signs of Potential Clinical Importance		SAC
32.	Safety	VS5	Listing of All Vital Signs for Subjects with any Value of Potential Clinical Importance		SAC

10.9.10. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Pharmacokinetics					
33.	PK Concentration	PKCL1P	Listing of GSK3640254 Plasma Concentrations (ng/mL) by Treatment – Cohort 1		SAC
34.	PK Concentration	PKCL1P	Listing of Darunavir Plasma Concentrations (ng/mL) by Treatment – Cohort 1		SAC
35.	PK Concentration	PKCL1P	Listing of Ritonavir Plasma Concentrations (ng/mL) by Treatment – Cohort 1		SAC
36.	PK Parameter	PKPL1P	Listing of GSK3640254 Plasma Pharmacokinetic Parameters Based on Actual Time by Treatment – Cohort 1		SAC
37.	PK Parameter	PKPL1P	Listing of Darunavir Plasma Pharmacokinetic Parameters Based on Actual Time by Treatment – Cohort 1		SAC
38.	PK Parameter	PKPL1P	Listing of Ritonavir Plasma Pharmacokinetic Parameters Based on Actual Time by Treatment – Cohort 1		SAC
39.	PK Concentration	PKCL1P	Listing of GSK3640254 Plasma Concentrations (ng/mL) by Treatment – Cohort 2		SAC
40.	PK Concentration	PKCL1P	Listing of Etravirine Plasma Concentrations (ng/mL) by Treatment – Cohort 2		SAC
41.	PK Parameter	PKPL1P	Listing of GSK3640254 Plasma Pharmacokinetic Parameters Based on Actual Time by Treatment – Cohort 2		SAC
42.	PK Parameter	PKPL1P	Listing of Etravirine Plasma Pharmacokinetic Parameters Based on Actual Time by Treatment – Cohort 2		SAC
43.	PK Concentration	PKCL1P	Listing of GSK3640254 Plasma Concentrations (ng/mL) by Treatment – Cohort 3		SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
44.	PK Concentration	PKCL1P	Listing of Darunavir Plasma Concentrations (ng/mL) by Treatment – Cohort 3		SAC
45.	PK Concentration	PKCL1P	Listing of Ritonavir Plasma Concentrations (ng/mL) by Treatment – Cohort 3		SAC
46.	PK Concentration	PKCL1P	Listing of Etravirine Plasma Concentrations (ng/mL) by Treatment – Cohort 3		SAC
47.	PK Parameter	PKPL1P	Listing of GSK3640254 Plasma Pharmacokinetic Parameters Based on Actual Time by Treatment – Cohort 3		SAC
48.	PK Parameter	PKPL1P	Listing of Darunavir Plasma Pharmacokinetic Parameters Based on Actual Time by Treatment – Cohort 3		SAC
49.	PK Parameter	PKPL1P	Listing of Ritonavir Plasma Pharmacokinetic Parameters Based on Actual Time by Treatment – Cohort 3		SAC
50.	PK Parameter	PKPL1P	Listing of Etravirine Plasma Pharmacokinetic Parameters Based on Actual Time by Treatment – Cohort 3		SAC
51.	Safety	PAN12	Listing of COVID-19 Assessments and Symptom Assessment		SAC
52.	Safety	AE9CP	Listing of Adverse Events of COVID-19		SAC