GlaxoSmithKline group of companies 208379

5Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)

Title	:	A Phase IIb, randomized, partially blind, active controlled, dose-range finding study of GSK3640254 compared to a reference arm of dolutegravir, each in combination with nucleoside reverse transcriptase inhibitors, in HIV-1 infected antiretroviral treatment-naive adults
Compound Number	:	GSK3640254
Clinical Study Identifier	:	208379
Effective Date	:	21 Jun 2023

Description:
The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Reports for Protocol 208379.
This RAP is intended to describe the efficacy, safety, PK required for the study at week 24 , up to Week 48 and Final End of Study (Eos) Analysis.
This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.
This version of the RAP documents the Sections considered as for this specific study as agreed by the study team.

RAP Author:

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Clinical Statistics & Clinical Programming Line Approvals
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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 208379. The RAP is based on the following 208379 protocol versions Amendment 04 -TMF-13994091 (01-Oct-2021).

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

This study was closed by the Sponsor after the Week 48 endpoint. All analyses associated with Weeks 96 and 144 have been removed from the study objectives and endpoints

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

Objectives	Endpoints
Primary Objective	**Primary Endpoints**
• To evaluate antiviral efficacy of GSK3640254 relative to DTG, each given in combination with 2 NRTIs, enabling the selection of an optimal dose for GSK3640254	• Proportion of participants with plasma HIV-1 RNA <50 copies/mL at Week 24 using the FDA snapshot algorithm
Secondary Objectives	**Secondary Endpoints**
• To evaluate antiviral efficacy in the Randomized Phase of GSK3640254 relative to DTG, each given in combination with 2 NRTIs at Week 48 •	• Proportion of participants with plasma HIV-1 RNA <50 copies/mL at Weeks 48 and 96 using the FDA snapshot algorithm • Absolute values and changes from baseline in HIV-1 RNA through Weeks 24, and 48Absolute values and changes from baseline in CD4+ cell counts through Weeks 24, and 48
• To evaluate safety and tolerability in the Randomized Phase of GSK3640254 relative to DTG each given in combination with 2 NRTIs at Weeks 24 and 48 •	• Frequency of SAEs, Deaths and AEs leading to Discontinuation through Weeks 24, and 48 • Incidence and severity of AEs through Weeks 24, and 48 • AEs in GI, Psych/CNS through Weeks 24, and 48
• To assess the development of viral resistance in the Randomized Phase to GSK3640254 and 2 NRTI backbone in participants experiencing virologic failure at Weeks 24 and 48.	• Changes in genotypic and/or phenotypic profiles of virus compared to baseline through Weeks 24, and 48

Objectives	Endpoints
• To characterize the pharmacokinetics of GSK3640254 when given in combination with ABC/3TC or FTC/TAF	• The steady-state plasma PK parameters of GSK3640254 will be assessed based on Intensive and/or Sparse PK sampling through Weeks 24 and 48

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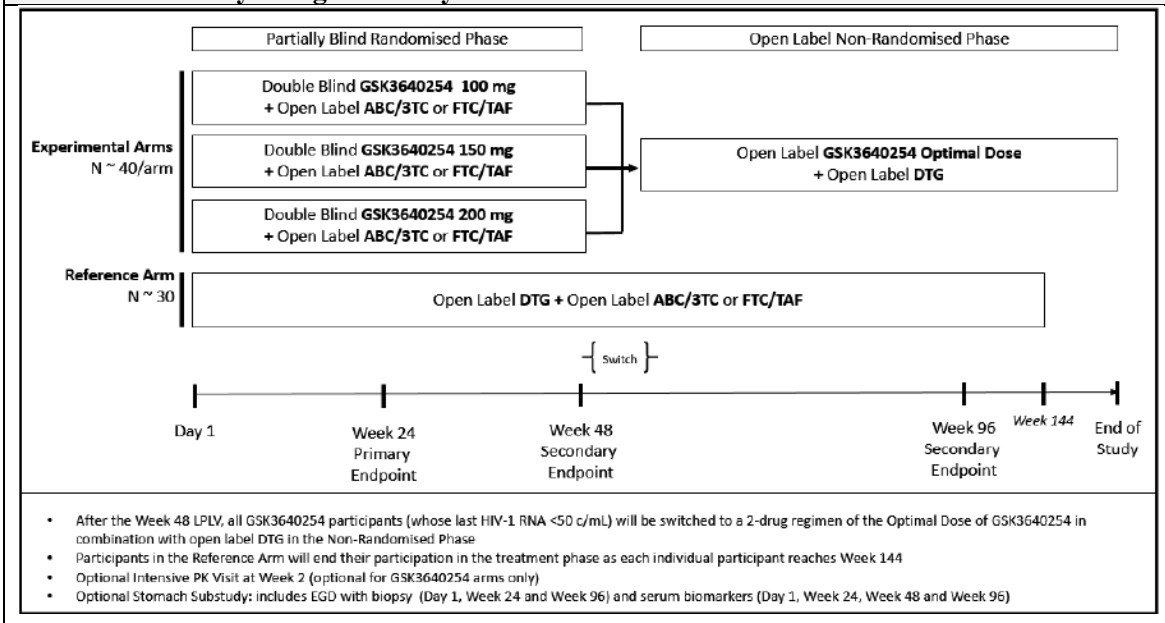
2.3. Study Design

Overview of Study Design and Key Features



Design Features	This trial is a multi-centre, adaptive, Phase IIb, randomized, partially blind (only to doses of GSK3640254), active controlled, dose-range finding study of GSK3640254 compared to a reference arm of dolutegravir, each in combination with nucleoside reverse transcriptase inhibitors, in HIV-1 infected antiretroviral treatment-naive adults.
Dosing	• Participants will take their randomized treatment once-daily throughout the course of the study
Time & Events	• Refer to Protocol Section 1.3
Treatment Assignment	• Participants will be randomized to either one of three doses (100 mg, 150 mg, or 200 mg) of GSK3640254, or DTG (50 mg) plus dual NRTI during the randomization phase. After the optimal dose has been chosen, and after the last participant completes their Week 48 visit, participants in the GSK3640254 arm will move into the Non-Randomised Phase receiving open label optimal dose and they will also be switched from the dual NRTI therapy to DTG. Participants in the control arm will continue with DTG (50 mg) plus dual NRTI until end of the study.
Interim Analysis	• One interim analysis will occur when 33% of planned enrolment (approximately 50 participants) have completed Week 12. This interim analysis will be conducted by an independent data monitoring committee to determine if any modifications to the trial would benefit participant safety.

2.4. Statistical Hypotheses / Statistical Analyses

The study is designed to investigate the antiviral activity, safety, and tolerability of three doses (100 mg, 150 mg, and 200 mg) of GSK3640254 given in combination with either ABC/3TC or FTC/TAF as compared to the reference treatment (defined as either DTG + ABC/3TC or DTG + FTC/TAF), and to select an optimal GSK3640254 dose for further development. Bayesian analyses will be conducted to evaluate the probability that the Week 24 response rate, defined as the proportion of participants with plasma HIV-1 RNA <50 c/mL as calculated by the FDA snapshot algorithm, of at least one dose of GSK3640254 has comparable efficacy to the reference treatment using a 10% margin.

3. PLANNED ANALYSES

3.1. Interim Analyses

An independent data monitoring committee (IDMC) will conduct an interim analysis after the 50th participant (33% enrolled) has completed their Week 12 visit. This interim analysis will be conducted to determine if any of the GSK3640254 doses are suboptimal and: 1) should be discontinued from the study or 2) if the entire study should be stopped due to futility. Full details of this analysis are contained in the IDMC charter.

3.2. Final Analyses

This study will have a primary analysis after all participants complete their Week 24 visit. There will be three additional subsequent analyses: after all participants complete their Week 48 Visit, and a End of study analysis at study completion. Each of these analyses will be performed after the completion of the following sequential steps:

All participants have completed their Week 24, 48 and the study (for the End of study analysis) as defined in the protocol.

All required database cleaning activities have been completed and final database lock (DBL) has been declared by Data Management.

For Week 24 all criteria for unblinding the randomization codes have been met.

For Week 24 analysis, randomization codes have been distributed according to RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• Comprises Screened for inclusion in the study, including screen-failures. • This population will be based on the treatment to which the subject was randomized. Screen-failures will be categorised as "non-randomized".	• Study Population
Randomized	• Any participant who has been randomized (for this study, this means a randomization number was assigned), whether or not the participant ever took a dose of study medication.	• Study Population
Safety	• All randomized participants who were exposed to study intervention with the exception of any participants with documented evidence of not having consumed any amount of study intervention • This population will be analysed according to the actual treatment the participant received.	• Demographic • Safety
Intent-To-Treat Exposed (ITT-E)	• All randomized participants who received at least one dose of study treatment. • Participants will be analyzed according to the randomized treatment regardless of what treatment was actually received	• Efficacy
Per-Protocol (PP)	• This population will consist of subjects in the ITT-E Population except for Important protocol deviations designated as exclusions from the analysis population. (see Section 14.1). • This population will be based on the treatment to which the subject was randomized. • Protocol deviations before a specified analysis timepoint that would exclude participants from the PP population are defined in Section 4.1 (Protocol Deviations) and Appendix 1: Exclusions from Per Protocol Population).	• Efficacy (Sensitivity analysis)

Population	Definition / Criteria	Analyses Evaluated
	E.g. a subject with an important protocol deviation between week 24 and Week48 would not be excluded due to this deviation from week 24 PP population but would be excluded from Week 48 PP population.	
Intent-To-Treat Exposed Sensitivity (ITT-ES)	• This population will consist of subjects in the ITT-E Population excluding any subjects with missing Week 24 data as a result of COVID-19 pandemic (this includes subjects that have discontinued due to COVID-19 before providing Week 24 data or still on study but no Week 24 Virologic data due to COVID-19. Note subjects with Week 24 Viral Load data and then discontinuing by COVID-19 subsequently will be included in the above table) • This population will be based on the treatment to which the subject was randomized.	• Efficacy (Sensitivity analysis)
Intensive Pharmacokinetic (Intensive PK)	• All participants who received at least one dose of GSK3640254 and have evaluable drug concentrations reported, where samples are collected according to the intensive PK sampling scheme Note: PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether the sample will be excluded.	• PK
Sparse Pharmacokinetic (Sparse PK)	• All participants who received at least one dose of GSK3640254 and have evaluable drug concentrations reported, where samples are collected according to the sparse PK sampling scheme • 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
Viral Genotypic	• Comprise of all subjects in the ITT-E population who have available On-treatment genotypic resistance data.	• Viral Genotypic

Population	Definition / Criteria	Analyses Evaluated
Viral Phenotypic	• Comprise of all subjects in the ITT-E population who have available On-treatment phenotypic resistance data.	• Viral Phenotypic
PDVF	• All subjects in the ITT-E population who met the PDVF criteria defined in the protocol. Please see Section 14.6.3for details of PDVF determination.	• Virology • Viral Genotypic • Viral Phenotypic
EGD sub study	• All subjects in the safety population who have consented to participate in the EGD sub study and have the baseline assessment.	•

Refer to Appendix 12: 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, patient management or patient assessment) will be summarised and listed.

Separately, important deviations which result in exclusion from analysis populations and events that result in exclusion from analysis populations will be summarised and listed.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan v3.0 (Latest version)

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

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		**Data Displays for Reporting**	
Code	**Description**	**Description**	**Order in TLF**
D1	GSK3640254 100mg	GSK254 100 mg + 2NRTIs	1
D2	GSK3640254 150mg	GSK254 150 mg + 2NRTIs	2
D3	GSK3640254 200mg	GSK254 200 mg + 2NRTIs	3
AC	Dolutegravir 50mg	DTG 50 mg + 2NRTIs	4

Treatment comparisons will be displayed as follows using the descriptors as specified:

- GSK254 100 mg + 2NRTIs vs DTG 50 mg + 2NRTIs
- GSK254 150 mg + 2NRTIs vs DTG 50 mg + 2NRTIs
- GSK254 200 mg + 2NRTIs vs DTG 50 mg + 2NRTIs

5.2. 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.

Parameter	**Study Assessments Considered as Baseline**		**Baseline Used in Data Display**
	Screening	**Day 1 (Pre-Dose)**	
Safety			
12-lead ECG	X	X	Day 1 (Pre-Dose)
Vital Signs	X	X	Day 1 (Pre-Dose)
Laboratory Assessments	X	X	Day 1 (Pre-Dose)
Efficacy			
HIV-1 RNA/ CD4+ T cell	X	X	Day 1 (Pre-Dose)
Virology			
Genotypic/ Phenotypic	X	X	Day 1 (Pre-Dose)

On Day 1 triplicate pre-dose ECGs will be performed. The baseline for every ECG parameter should calculated as the average of that parameter's values from the Day 1 pre-dose triplicate ECG reading.

On Day 1 three readings of blood pressure and pulse will be taken. The first reading should be rejected. The average of the second and third readings (as recorded in the CRF) will serve as baseline.

For Genotypic and Phenotypic data, Day 1 visit data will serve as baseline, otherwise, baseline will be set to missing.

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

5.3. Multicentre Studies

In this multicentre global study, enrolment will be presented by country and investigative site. For purposes of efficacy analyses, all sites are assumed to be exchangeable and there will be no site or country level adjustment.

5.4. Examination of Covariates, Other Strata and Subgroups

5.4.1. Covariates and Other Strata

The list of covariates and other strata may be used in descriptive summaries and statistical analyses, some of which may also be used for subgroup analyses. Additional covariates and other strata of clinical interest may also be considered.

Category	Details
Randomization Strata using Baseline Values	The randomization is stratified by factors which are assessed using screening values. The baseline categories are considered to be more relevant, hence the randomization strata are re-derived using baseline values and will be referred to as the analysis strata. Strata will be based on actual data as opposed to data from the randomization system. The strata are as follows: • Screening HIV-1 RNA (<100,000 copies/mL or >=100,000 copies/mL) • Initial background dual NRTI (ABC/3TC or FTC/TAF),
Covariates	• Baseline HIV-1 RNA (<100,000 copies/mL, 100,000 to < 250,000 copies/mL, 250,000 to < 400,000 copies/mL, 400,000 to < 500,000 copies/mL, >= 500,000 copies/mL) • Background dual NRTI (ABC/3TC or FTC/TAF, Others) at week 24 or time of IP discontinuation, whichever is earlier • Baseline CD4+ cell count, (≤200 cells/mm^3 or >200 cells/mm^3)

Category	Details
	• Baseline CDC category (HIV infection stage 0, HIV infection stage 1, HIV infection stage 2, HIV infection stage 3 (AIDS), HIV infection stage unknown) • Race (White, Black, Asian, Other) • Sex (Female, Male)

5.4.2. Examination of Subgroups

The list of subgroups may be used in descriptive summaries and statistical analyses. Additional subgroups of clinical interest may also be considered.

- If the percentage of participants is small within a particular subgroup, then the subgroup categories may be refined prior to unblinding the trial.
- If the category cannot be refined further, then descriptive rather than statistical comparisons may be performed for the particular subgroup.
- Descriptive summaries of subgroups will only include subjects with non-missing data. The number of subjects with non-missing data for each subgroup will be displayed in the table (n) and be used as the denominator in percent calculations.

Subgroup	Categories
Baseline HIV RNA	• <100,000 copies/mL • >=100,000 copies/mL
Baseline NRTI	• ABC/3TC • FTC/TAF
Age	• <50 years • ≥50 years OR • <35 • 35-<50 • ≥50
Race	• White • Black • Asian • Other OR • White • Non-White
Sex	• Female • Male
Baseline CD4+ Cell Count (cells/mm3)	• <200 • 200 to <350 • 350 to <500 • ≥500

Subgroup	Categories
History of Depression or Psychiatric Events at Baseline	• Yes • No
BMI	• Underweight • Normal • Overweight • Obese

NOTES: **Underweight = BMI of < 18.5 kg/m2, Normal = BMI of 18.5 – 24.99 kg/m2, Overweight = BMI of 25 – 29.99 kg/m2, Obese = BMI of ⩾ 30 kg/m2.**

5.5. Multiple Comparisons and Multiplicity

The study is designed to select a dose primarily on the basis of antiviral activity and tolerability in conjunction with immunological response, safety, and pharmacokinetic measures and is not designed to evaluate formal statistical hypotheses. Hence, adjustments for multiplicity are not applicable.

5.6. 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
Section14.1	Appendix 1: Exclusions from Per Protocol Population
Section14.2	Appendix 2: Schedule of Activities
Section14.3	Appendix 3: Assessment Windows
Section14.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
Section14.5	Appendix 5: Data Display Standards & Handling Conventions
Section14.6	Appendix 6: Derived and Transformed Data
Section14.7	Appendix 7: Reporting Standards for Missing Data
Section14.8	Appendix 8: Values of Potential Clinical Importance
Section14.9	Appendix 9: Population Pharmacokinetic
Section14.10	Appendix 10: Time to Event Details
Section14.11	Appendix 11: Abbreviations and Trademarks
Section14.12	Appendix 12: List of Data displays
Section14.13	Appendix 13: Example Mock shells

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the “Screened”, “Randomized”, Intent-to-Treat Exposed population, unless otherwise specified.

Study population analyses including analyses of participant’s disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and exposure and treatment compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 12: List of Data Displays.

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

This study is designed to investigate the antiviral activity of three doses (100 mg, 150 mg, and 200 mg) of GSK3640254 given in combination with either ABC/3TC or FTC/TAF as compared to the reference treatment of DTG+ABC/3TC or DTG+FTC/TAF, and to select an optimal dose of GSK3640254 for further development. To achieve this objective, a Bayesian analysis will be conducted to evaluate the probability that the Week 24 response rate, defined as the proportion of participants with plasma HIV-1 RNA < 50 c/mL as calculated by the FDA snapshot algorithm, of at least one dose of GSK3640254 has comparable efficacy to the reference treatment using a 10% margin. A positive efficacy decision will be made if any GSK3640254 dose has a high posterior probability (e.g. >= 0.85) of being within the 10% margin.

7.1.1. Endpoint / Variables

The primary efficacy endpoint is the binary outcome indicating the virologic category of plasma HIV-1 RNA <50 copies/mL (c/mL) at Week 24 using the FDA Snapshot algorithm (See Section 14.6.3.1). The other Snapshot outcomes (HIV-1 RNA ≥50 copies/mL (c/mL) and no virologic data at Week 24 Window) will be collapsed into a single category for the analysis (non-response category).

7.1.2. Summary Measure

For each dose of GSK3640254 the following Bayesian statistics will be provided:

- The number and proportion of subjects with plasma HIV 1 RNA <50 copies c/mL at Week 24 using the snapshot algorithm.
- Summary statistics of the posterior distribution of response rate for the specified dose including:
    - Mean, median, and mode of posterior distribution of response rate for the specified dose
    - 95% highest posterior density credible interval of response rate for the specified dose

For the control arm the following Bayesian statistics will be provided:

- The number and proportion of subjects with plasma HIV 1 RNA <50 copies c/mL at Week 24 using the snapshot algorithm
- Summary statistics of the posterior distribution of response rate for the control including:
    - Mean, median, and mode of posterior distribution of response rate

- 95% highest posterior density credible interval of response rate

- Posterior Probability that response rate of the specified dose is greater than the control arm response rate -10%. That is:

    - Posterior Pr(Response rate GSK3640254 XX mg – Response Rate Control) > -0.1

For each dose, this posterior probability will be compared to 85% to determine if that dose achieves internal sponsor go/no-go decision-making criteria for efficacy

Main analytical approach

Comparisons between dose arms will be made by calculating differences between the posterior distributions of the response rate in each arm with the control arm which will be summarized to obtain posterior means and CIs. Samples from the posterior distribution of the response rates in each arm will also be used to obtain posterior probabilities of interest (e.g. Pr(Response rate GSK3640254 XX mg – Response Rate Control arm > -10% | Data)).The point estimates of differences in virologic response rate with 95% credible intervals will be calculated for the treatment comparisons described in the estimands.

Posterior probability for the differences of following comparisons will also be reported.

1. Response rate GSK3640254 100 mg vs. Response Rate Control arm
2. Response rate GSK3640254 150 mg vs. Response Rate Control arm
3. Response rate GSK3640254 200 mg vs. Response Rate Control arm

If success criteria are met for more than one arm, then additional factors would be taken into consideration.

7.1.3. Population of Interest

The primary efficacy analyses will be based on the Intent-to-Treat Exposed (ITT-E) and Per Protocol Population for sensitivity analysis.

7.1.4. Strategy for Intercurrent (Post-Randomization) Events

Intercurrent events such as discontinuations, missing plasma HIV-1 RNA samples and change in background regimen are handled using the Snapshot algorithm (see Section 14.6.3.1), which details how to assign each participant’s virologic outcome.

7.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 12: 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 summarised using descriptive statistics, graphically presented (where appropriate) and listed.

7.1.5.1. Primary Endpoint Statistical Methodology Specification

Endpoint / Variables

- Binary outcome indicating the virologic category of plasma HIV-1 RNA <50 copies/mL (c/mL) at Week 24 using the FDA Snapshot algorithm

Model Specification

- Posterior distributions of the response rates for each dose, d, of GSK3640254 and the reference treatment will be calculated according to the following Bayesian model and parameters:
- $p_d = probability\ of\ response\ on\ dose\ d$

$$p_d = \frac{e^{\theta_d}}{1 + e^{\theta_d}}$$

- $\theta_d = Log\ odds\ of\ probability\ of\ response\ for\ dose\ d$

$$\theta_d = \ln\left(\frac{p_d}{1 - p_d}\right)$$

- Prior for the log odds of response on GSK3640254 arms

$$\theta_d \sim N(0,5^2)$$

- Prior for the log odds of response of the DTG reference arm

$$\theta_{DTG} \sim N(2.61, 0.7324^2)$$

Model details:

A Bayesian hierarchical model will be fitted using MCMC methods, and will be used to estimate the posterior probability of virologic response rate(Week 24 response rate, defined as the proportion of participants with plasma HIV-1 RNA < 50 c/mL as calculated by the FDA snapshot algorithm) for each arm incorporating the baseline analysis stratification factors defined below*Jones, 2011*

Baseline Analysis Strata

Stratum	B_1: Baseline HIV-1 RNA ($I_{\{B1+\}}$)	B_2: Initial background dual NRTI ($I_{\{B2+\}}$)
<100,000 copies/mL AND ABC/3TC	B_{1-}(<100,000 c/mL) (0)	B_{2-} (ABC/3TC) (0)
≥100,000 copies/mL AND ABC/3TC	B_{1+}(≥100,000 c/mL) (1)	B_{2-} (ABC/3TC) (0)
<100,000 copies/mL AND FTC/TAF	B_{1-}(<100,000 c/mL) (0)	B_{2+} (FTC/TAF) (1)
≥100,000 copies/mL AND FTC/TAF	B_{1+} (≥100,000 c/mL) (1)	B_{2+} (FTC/TAF) (1)

Model for each arm:

$$Number\ of\ responders\ r_g \sim Binomial(n_g, p_g), \qquad g = 1,2,3,4$$

$$\theta_g = logit(P_g) = \log\left(\frac{P_g}{1-P_g}\right) = \gamma_0 + \gamma_1 I_{\{B1+\}} + \gamma_2 I_{\{B2+\}} + \psi_g, \qquad g = 1,2,3,4$$

Where $\gamma_0,\ \gamma_1,\ \gamma_2,\ \psi_g$ are all parameters. Thus,

$\theta_1 = \gamma_0 + \psi_1$

$\theta_2 = \gamma_0 + \gamma_1 + \psi_2$

$\theta_3 = \gamma_0 + \gamma_2 + \psi_3$

$\theta_4 = \gamma_0 + \gamma_1 + \gamma_2 + \psi_4$

Priors:

$\gamma_k \sim Normal\left(0, 10^6\right), k = 0,1,2$

$\psi_g \sim Normal(0, \omega^2), g = 1,2,3,4$

$\omega \sim Half - normal(1)$

Where we define r_g as the number of Virologic responders among n_g participants, p_g as Virologic response rate $\frac{r_g}{n_g}$, θ_g as the log odds of treatment response $\log(\frac{p_g}{1-p_g})$, index g =1,...,4 refers to the analysis stratum number, γ_k represent fixed effects of baseline analysis stratification factors (see below), and ψ_g denotes a random effect in analysis stratum g.

The four analysis strata and representation of the two baseline analysis stratification factors B_1 and B_2 in the model are shown in Table above.

For each arm, the posterior distribution of Virologic response rate $P(p_g|data)$, g=1,2,3,4 will be derived for each analysis stratum using the model specified above.

$$P(p_1|data) = P(\frac{e^{\theta_1}}{1+e^{\theta_1}}|data)$$

$$P(p_2|data) = P(\frac{e^{\theta_2}}{1+e^{\theta_2}}|data)$$

$$P(p_3|data) = P(\frac{e^{\theta_3}}{1+e^{\theta_3}}|data)$$

$P(p_4|data) = P(\frac{e^{\theta_4}}{1+e^{\theta_4}}|data)$

The posterior distribution of the arm-level Virologic response rate will be derived using a mixture of the posterior distributions of Virologic response rate for each analysis stratum in that arm. The weights are proportional to the sample size of each analysis stratum in each arm.

$P(p|data) = \sum_{g=1}^{4} w_g P(p_g|data)$, where $w_g = \frac{n_g}{\sum_{g=1}^{4} n_g}$

Model Checking & Diagnostics

- Specific model checking procedures will be implemented according to the "Bayesian Statistics Best Practice at GSK- Clinical Trials Using Bayesian Inference document.

Model Results Presentation

- A figure will be produced which displays the posterior distribution of response rate for each of the dose of GSK3640254 as well as the posterior distribution of response rate for the DTG control arm.
- The mean of the posterior distribution of Week 24 snapshot response rate as well as associated 95% highest posterior density credible interval will be calculated for each dose of GSK3640254 and the reference DTG arm and presented in tabular form

Sensitivity Analyses

- Per-Protocol population analysis: To assess the impact of significant protocol deviations, statistical analysis will be repeated using the Per-Protocol population and compared for consistency with the results from the primary ITT-E population analysis.
- The binary response indicating the virologic outcome category of plasma HIV-1 RNA <50 copies/mL (c/mL) at 24, using the FDA Snapshot algorithm: Adjusted Difference using CMH estimate in the percent of subjects with plasma HIV 1 RNA<50 c/mL at Week 24, defined by the FDA snapshot algorithm between Active treatment groups (Each arm of GSK'254 combination doses) vs Control arm. For the analysis details please see Section 7.2.5.1.

Number and percent of participants with plasma HIV-1 RNA <50 copies/mL (c/mL) at Week 24, using the FDA Snapshot algorithm, will be also tabulated by treatment with Clopper Pearson 95% confidence intervals also presented graphically.

7.2. Secondary Efficacy Analyses

7.2.1. Endpoint / Variables

Secondary analyses will be conducted on:

- The binary outcome indicating the virologic category of plasma HIV-1 RNA <50 copies/mL (c/mL) at Weeks 48 and 96 using the FDA Snapshot algorithm (See Section 14.6.3.1). The other Snapshot outcomes (HIV-1 RNA ≥50 copies/mL (c/mL) and no virologic data in the Week 48 and 96 Windows) will be collapsed into a single category for the analysis.
- Absolute values and changes from baseline in HIV-1 RNA through Weeks 24, 48, and 96
- Absolute values and changes from baseline in CD4+ T-cell counts through Weeks 24, 48, and 96
- CD4+/CD8+ cell count ratio at weeks 24, 48 and 96.
- Incidence of disease progression (HIV-associated conditions, AIDS, and death) through weeks 24, 48 and 96

7.2.2. Summary Measure

Percent of participants with plasma HIV-1 RNA <50 copies/mL (c/mL) at Weeks 48 and 96, defined by the FDA Snapshot algorithm (see Section 14.6.3.1), between each treatment group (GSK3640254 –DTG).

Descriptive statistics (mean, median, standard deviation, etc.) of absolute values and changes from baseline in HIV-1 RNA, Log10 of HIV-1 RNA, CD4+ T-cell counts, CD4+/CD8+ cell count ratio through weeks 24, 48, and 96. Incidence of disease progression (HIV-associated conditions, AIDS, and death) through weeks 24, 48 and 96.

7.2.3. Population of Interest

The secondary efficacy analyses will be based on the Intent-to-Treat Exposed (ITT-E) , unless otherwise specified.

7.2.4. Strategy for Intercurrent (Post-Randomization) Events

Intercurrent events such as discontinuations, missing plasma HIV-1 RNA samples and change in background regimen are handled using the Snapshot algorithm (see Section 14.6.3.1), which details how to assign each participant's virologic outcome.

7.2.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 12: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 7.2.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

There will not be any formal statistical analysis of secondary endpoints. Only descriptive statistics will be reported.

7.2.5.1. Statistical Methodology Specification

Endpoint / Variables

The binary response indicating the virologic outcome category of plasma HIV-1 RNA <50 copies/mL (c/mL) at weeks 48, and 96, using the FDA Snapshot algorithm (see Section 14.6.3.1),

Model Specification

The efficacy endpoint will be analysed using a stratified analysis for proportions with Cochran-Mantel-Haenszel (CMH) weights, adjusting for Baseline HIV-1 RNA (<100,000 copies/mL or ≥100,000 copies/mL) and the investigator's choice of dual NRTI background therapy (ABC/3TC or FTC/TAF). Details of the analysis strata can be found in the Section 5.4.1. The CMH estimate of the adjusted treatment difference will be calculated as a weighted average of strata-specific estimates of the treatment difference calculated within each of the following 4 analysis strata:

- <100,000 copies/mL AND ABC/3TC
- <100,000 copies/mL AND FTC/TAF
- ≥100,000 copies/mL AND ABC/3TC
- ≥100,000 copies/mL AND FTC/TAF

If n_k is the number of Treatment treated participants, m_k is the number of Comparator treated participants, and $N_k = n_k + m_k$ is the total number of participants in the kth stratum, then the CMH estimate is given by

where,

$$W_k = \frac{n_k m_k}{N_k}$$

are CMH weights and d_k are estimates of the differences in proportions of participants with plasma HIV-1 RNA <50 copies/mL (c/mL) between the two treatment arms (Doses of GSK3640254), $r_{GSK3640254} - r_{DTG}$, for the kth strata.

The corresponding two-sided 95% CI will be calculated as

$$\hat{d}_{cmh} \pm 1.96 \times \sqrt{\hat{\text{var}}(\hat{d}_{cmh})}$$

where the variance estimator (Sato, 1989) is consistent in both sparse data and large strata and is given below

$$\hat{\text{var}}\left(\hat{d}_{cmh}\right) = \frac{\hat{d}_{cmh}\left(\sum P_k\right) + \sum Q_k}{\left(\sum n_k m_k / N_k\right)^2} = \frac{\hat{d}_{cmh}\left(\sum P_k\right) + \sum Q_k}{\left(\sum W_k\right)^2}$$

where

$$P_k = \frac{n_k^2 y_k - m_k^2 x_k + n_k m_k (m_k - n_k)/2}{N_k^2}$$

$$Q_k = \frac{x_k(m_k - y_k)/N_k + y_k(n_k - x_k)/N_k}{2}$$

with x_k and y_k corresponding to the number of participants with HIV-1 RNA <50 copies/mL (c/mL) at weeks 48, ad 96 as determined by the FDA Snapshot algorithm (see Section 14.6.3.1), for treatment and comparator, respectively, for the kth stratum.

Model Checking & Diagnostics

- Not applicable, as no formal statistical modeling is being performed

Model Results Presentation

Adjusted CMH estimate of the difference in the percent of participants with plasma HIV-1 RNA <50 copies/mL (c/mL) between each treatment group (GSK3640254–DTG) and corresponding 95% confidence interval will be presented.

Subgroup Analyses

- An analysis for subgroups listed in Section 5.4.2 will be performed. This will show the percent of participants with plasma HIV-1 RNA <50 copies/mL (c/mL) at the time of analysis (Weeks 24 and 48) based on the Snapshot algorithm (Section 14.6.3.1) and will be presented by treatment group. Unadjusted percent by subgroup and corresponding two-sided 95% (Wilson Score) confidence intervals will be tabulated and may also presented graphically in a forest plot.

Percent of participants with HIV-1 RNA <50 copies/mL (c/mL) will be also tabulated by treatment and visit with Wilson 95% confidence intervals.

8. Virology

8.1. Overview of Planned Virology Statistical Analysis

The virology analyses of genotype and phenotype data will be based on the Viral Genotypic, Phenotypic and PDVF populations with subjects having Viral load >= 200 c/ml.

The PDVF population will be based on subjects who have experienced a PDVF at any point. Refer to protocol Section 7.1.1 and Section 4.1.2.2.1 and RAP Section 14.6.4 for the details of the PDVF details. Summary tables will present PDVFs up to and including the time point of interest. PDVFs must be confirmed within the phase in which they are reported. Listings will present PDVFs occurring at any point.

Full sequence reverse transcriptase (RT), integrase inhibitors (INI), protease inhibitors (PI), and the study drug GSK3640524 maturation inhibitors (MI) available data will be analysed at baseline, Week 4, and at time of confirmed protocol-defined virologic failure for baseline mutations and for emergent mutations. Additionally, genotypic changes from baseline will be identified and listed to potentially identify pathways to resistance. These analyses will use the PDVF population.

Phenotypic changes for approved drugs will be determined at baseline, Week 4, and at time of confirmed PDVF. Emergent phenotypic changes will be investigated in the on-treatment Genotypic and Phenotypic population.

Details of data displays is presented in Appendix 12: List of Data Displays.

9. SAFETY ANALYSES

The safety analyses will be based on the Safety population, unless otherwise specified. Relevant COVID-19 tables, figures, and listings will be included as described by GSK standards.

9.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 12: List of Data Displays.

Adverse events will be summarized using descriptive statistics and will not undergo formal statistical analysis. Selected adverse events summaries may also be reported by NRTI backbone to explore any potential relationship.

9.2. Adverse Events of Special Interest Analyses

A comprehensive list of MedDRA terms based on clinical review will be used to identify each type of event in a separate document (AESI MedDRA). Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from ongoing studies may highlight additional adverse events of special interest, therefore the list of terms to be used for each event of interest and the specific events of interest are defined at a compound level and based on the safety review team (SRT) agreements in place at the time of reporting.

Current AESI categories are as follows:

- QT prolongation
- GI intolerability/toxicity
- Psychiatric Events
    - Suicidal ideation/behavior
    - Depression
    - Bipolar Disorder
    - Psychosis
    - Anxiety
    - Sleep Disorders
- Nervous System Disorders
- Skin and subcutaneous tissue disorders

The details of the planned displays are provided in Appendix 12: List of Data Displays.

Adverse events of special interest will be summarized using descriptive statistics and will not undergo formal statistical analysis.

9.3. Clinical Laboratory and Biomarker Analyses

Laboratory evaluations including the analyses of chemistry laboratory tests, hematology laboratory tests, urinalysis, liver function tests, and pregnancy tests will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 12: List of Data Displays.

All parameters are listed in Table 13 of Section 10.2 of the protocol.

The following descriptive summaries for data will be provided:

N (number of subjects in the population), n (number of subjects used for the analysis), arithmetic mean, 95% CI for the arithmetic mean, SD, median, minimum, maximum for the untransformed data.

9.3.1. Lipids

Statistical Analyses
Endpoints
• Change from Baseline in Fasting Lipids (Triglycerides, LDL cholesterol, HDL cholesterol, Total Cholesterol and TC/HDL ratio) at Weeks 24 and 48
Analysis Specification
• The data will not be log transformed for the lipids and will be presented on the normal scale.
Results Presentation
• N (number of subjects in the population), n (number of subjects used for the analysis), arithmetic mean, 95% CI for the arithmetic mean, SD, median, minimum, maximum will be presented for the untransformed data.

9.3.2. CCI [redacted], Insulin, Glucose and HbA1c Analyses

Analyses
Endpoints
• Change from baseline in CCI [redacted], Insulin, Glucose and HbA1c at Weeks 24 and 48. Please refer to Section 14.6.5for the details.
Analysis Specification
• If change in CCI [redacted], Insulin, Glucose or HbA1c is not normally distributed the data will be log transformed
Results Presentation
• N (number of subjects in the population), n (number of subjects used for the analysis), arithmetic mean, 95% CI for the arithmetic mean, SD, Q1, Q3, median, minimum, maximum will be presented for the untransformed data.

Analyses
For the log transformed parameters, geometric means will replace arithmetic means, a 95% CI will replace the standard deviations.

9.3.3. Bone Biomarkers Analyses

Analyses
Endpoints
• Change from baseline in the following bone biomarkers at Weeks 24 and 48: o bone-specific alkaline phosphatase o procollagen type 1 N-propeptide o type 1 collagen cross-linked C-telopeptide o osteocalcin o 25 hydroxy-Vitamin D
Analysis specification
• It is anticipated that bone biomarkers will be normally distributed and for those, the data will not be log transformed
Results Presentation
• N (number of subjects in the population), n (number of subjects used for the analysis), arithmetic mean, SD, median, Q1, Q3, minimum, maximum will be presented.

9.3.4. Renal Biomarkers Analyses

Analyses
Endpoints
• Change from baseline in the following renal biomarkers at Weeks 24 and 48: o Cystatin C (blood) o Retinol Binding Protein (RBP, urine) o Beta-2-Microglobulin (B2M, urine) o Urine RBP/creatinine ratio o Urine B2M/creatinine ratio o urine albumin/creatinine ratio o urine protein/creatinine ratio o urine phosphate o serum creatinine o eGFR (based on CKD-EPI-creatinine) o eGFR (based on CKD-EPI-cystatin C)
Analysis Specification
• It is anticipated that at least some biomarkers will not be normally distributed and for those, the data will be log transformed
Model Results Presentation

Analyses
• N (number of subjects in the population), n (number of subjects used for the analysis), arithmetic mean, SD, Q1, Q3, median, minimum, maximum will be presented for the untransformed data.   • For the log transformed parameters, geometric means will replace arithmetic means, a 95% CI will replace the standard deviations.

9.3.5. Inflammatory Biomarkers Analyses

Analyses
Endpoints

• Change from baseline in the following inflammatory biomarkers at Weeks 24 and 48:
  o Interleukin-6 (IL-6)
  o High-sensitivity C reactive protein (hs-CRP)
  o D-dimer
  o Soluble CD14 (sCD14)
  o Soluble CD163 (sCD163)

Analysis Specification
• It is anticipated that inflammatory biomarkers will not be normally distributed and for those, the data will be log transformed and geometric means will replace arithmetic means, a 95% CI will replace the standard deviations and mean changes from baseline will be presented as geometric mean ratios.
Results Presentation
• For the log transformed data, geometric means will replace arithmetic means, a 95% CI will replace the standard deviations and median, Q1, Q3, minimum and maximum will be presented.

9.3.6. Stomach/Gastric Biomarkers

Statistical Analyses
Endpoints

• Absolute and change from baseline in the following gastric biomarkers at Weeks 24 and 48:
  o Fasting Gastrin
  o Pepsinogen I
  o Pepsinogen II

Results Presentation
• Summary statistics (absolute and change from baseline) will be provided by treatment arm for each of the serum gastric biomarkers (gastrin and pepsinogen I and II) for participants in the EGD sub-study.
Results Presentation

Statistical Analyses
• N (number of subjects in the population), n (number of subjects used for the analysis), arithmetic mean, 95% CI for the arithmetic mean, SD, median, Q1, Q3, minimum, maximum will be presented.

The details on histopathologic findings on Esophagogastro- duodenoscopy (EGD) with biopsy and Gastric Biopsy findings (PRF) will be summarized using Tables and Listings. Those have been included in the Appendix 12: List of Data Displays.

9.4. Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs, vital signs, liver events, Columbia Suicide Severity Rating Scale (C-SSRS), and gastrointestinal intolerability evaluation and monitoring (if available), will be based on GSK Core Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 12: List of Data Displays.

A summary of subjects meeting hepatobiliary laboratory abnormality criteria at any post-Baseline emergent visit will also be produced based on FDA Guidance for Drug-Induced Liver Injury: Premarketing Clinical Evaluation (July 2009). In addition, a summary and listing of subjects with Liver Stopping Events will also be produced.

10. PHARMACOKINETIC ANALYSES

10.1. Endpoint / Variables

10.1.1. Drug Concentration Measures

All PK concentration listing displays will be based on the Intensive and Sparse Pharmacokinetic populations. Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 14.5.3 Reporting Standards for Pharmacokinetic). GSK3640254 concentration listings for the intensive PK population will be sorted by subject and time relative to dose, noting the study visit; summaries will be presented by study visit and time relative to dose.

GSK3640254 concentration listings for the sparse PK population will be sorted by subject, study visit and time (or sampling window) relative to dose; summaries will be presented by study visit and time (or sampling window) for weeks 4, 8, 12, 24, 36, and 48.

10.1.2. Derived Pharmacokinetic Parameters for Subjects Participating in the Intense PK

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin. All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters at Week 2 (or week 16 if participants cannot take part in week 2 intensive PK) listed will be determined from the concentration-time data, as data permits. Ctau will be estimated from pre-dose concentration for all subjects in the Sparse PK population.

Parameter	Parameter Description
$AUC_{(0\text{-}tau)}$	Area under the concentration-time curve over the dosing interval. AUC will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid
C_{max}	Maximum observed plasma concentration
C_{tau}	Observed plasma concentration at the end of the dosing interval, determined directly from the concentration-time data
C_0	Observed pre-dose plasma concentration, determined directly from the concentration-time data
T_{max}	Time to C_{max}, determined directly from the concentration-time data
CL/F	Oral clearance, the apparent volume of plasma cleared of GSK3640254 per unit time following extravascular dosing, calculated as: $CL/F = Dose / AUC_{(0\text{-}tau)}$

10.2. Summary Measure

All derived PK parameters detailed in Derived Pharmacokinetic Parameters section will be summarized by treatment and subgroups; baseline plasma HIV RNA (<100,000, ≥100,000 copies/mL) and the investigator's choice of dual NRTI background therapy (ABC/3TCor FTC/TAF) and overall.

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11. POPULATION PHARMACOKINETIC (POPPK) ANALYSES

A population-based PK model may be constructed based on the GSK3640254 intensive concentration PK data at weeks 2, and the sparse concentrations PK data collected at weeks 4, 8, 12, 24, 36, and 48, if the quality of the data permits. Data from the study could be merged with some previous data to help the model building process. The influence of subject demographics, baseline characteristics, including disease activity, and co-medication on the pharmacokinetics of GSK3640254 in this population may be explored. The individual subject PK parameters will be estimated and documented for the purposes of any subsequent exposure response (PK/PD) analyses. The PopPK analyses for GSK3640254 will be performed under a separate RAP and will be reported separately.

Further details to be included in a separate RAP.

12. PHARMACOKINETIC / PHARMACODYNAMIC ANALYSES

The primary goal of this analysis is to characterize the pharmacokinetic / pharmacodynamic relationship of GSK3640254 administered orally in HIV-1 infected participants. The influence of participant demographics and baseline characteristics, including disease activity in this population will be investigated.

Further details to be included in a separate RAP.

13. REFERENCES

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14. APPENDICES

14.1. Appendix 1: Exclusions from Per Protocol Population

A participant meeting any of the following criteria will be excluded from the Per-Protocol population:

Number	Exclusion Description
01	Subject deviates from any inclusion or exclusion criteria, as recorded in the eCRF
02	Subject took/received incorrect study treatment (MI254+2NRTI or DTG+2NRTI), i.e., other than the one to which they were randomized for more than 10% of the total time On-treatment
03	Interruption/Dose modification of randomized regimen (MI254+2NRTI or DTG+2NRTI) for longer than 10% of the total time on-treatment for reasons other than treatment related adverse events/laboratory abnormalities. Derivation will be based on concomitant medication and IP eCRF forms.
04	Prohibited medications: receiving ART medication other than that prescribed/allowed by the study for more than 7 days or receiving prohibited Concomitant medication that would impact exposure or response to therapy with duration taken into consideration. The following, general concomitant medications or therapies are not permitted at any time during the study: • HIV immunotherapeutic vaccines are not permitted at any time during the study. • Other experimental agents, antiretroviral drugs not otherwise specified in the protocol, cytotoxic chemotherapy, or radiation therapy may not be administered. • Systemically administered immunomodulators (such as interleukin and interferon agents) are prohibited (a list of examples is provided in the SRM) This includes topical agents with substantial systemic exposure and systemic effects. Use of topical imiquimod is permitted. • Acetaminophen (paracetamol) cannot be used in patients with acute viral hepatitis. Note: For treatment specific prohibited meds refer in Section 6.8.1.3. and Section 6.8.1.4. of the protocol
05	Permanent discontinuation of IP/withdrawal due to a reason of “Protocol Deviation” (as recorded in the eCRF).

14.2. Appendix 2: Schedule of Activities

14.2.1. Protocol Defined Schedule of Events

Refer to Protocol Section 1.3.

14.3. Appendix 3: Assessment Windows

14.3.1. Definitions of Assessment Windows for Snapshot Analyses

Analysis Set / Domain	Parameter (if applicable)	Target (Day)	Analysis Window (Day)		Analysis Timepoint	Window Weeks
			Beginning Timepoint	Ending Timepoint		
Efficacy	Snapshot Endpoint	-63		<-3	Screen	NA
		1	-3	1	Day 1	NA
		15	2	21	Week 2	Day 2 ~ Week 3
		29	22	42	Week 4	3~6
		57	43	70	Week 8	6~10
		85	71	98	Week 12	10~14
		113	99	126	Week 16	14~18
		169	**127**	**210**	**Week 24**	**18-30**
		225	211	238	Week 32	30~34
		253	239	266	Week 36	34~38
		281	267	294	Week 40	38~42
		337	**295**	**378**	**Week 48**	**42-54**
		393	379	420	Week 56	54~60
		449	421	476	Week 64	60~68
		505	477	532	Week 72	68~76
		561	533	588	Week 80	76~84
		617	589	630	Week 88	84~90
		673	**631**	**714**	**Week 96**	**90-102**
		X*7+1	(X-6)*7+1	(X+6)*7	Week X, X=108, 120, 132, etc	(X-6)~(X+6)
		Study Day of last dose + 28	>= (Study Day of last dose + 28)		Follow-up	NA

NOTES:

1. The Snapshot visit windows are used as part of the Snapshot algorithm to determine a participant's category.
2. Week 24, 48, and 96 follow FDA Snapshot Algorithm to use +/- 6 weeks as the analysis window. Apply Snapshot analysis windows only to viral load data that is on-treatment
3. Other analyses visits will use analysis windows ½ the distance between the previous and subsequent timepoint.

14.3.2. Definitions of Assessment Windows for Other Analyses

Other analyses Sets (e.g. lab) will use analysis windows ½ the distance between the previous and subsequent timepoint.

Analysis Set / Domain	Parameter (if applicable)	Target (Day)	Analysis Window (Day)		Analysis Timepoint	Window Weeks
			Beginning Timepoint	Ending Timepoint		
Efficacy (Observed)/Safety (Lab, ECG, VS)/Virology[1]	All	-63		<-3	Screen	NA
		1	-3	1	Day 1	NA
		15	2	21	Week 2	Day 2 ~ Week 3
		29	22	42	Week 4	3~6
		X*7+1	(X-2)*7+1	(X+2)*7	Week X, X=8, 12, … , 52, once every 4 weeks from Week 8 to 52	(X-2) ~(X+2)
		393	379	420	Week 56	54~60
		X*7+1	(X-4)*7+1	(X+4)*7	Week X, X=64, 72, …, 88, every 8 weeks from week 64 to 88	(X-4)~(X+4)
		673	645	714	Week 96	92~102
		X*7+1	(X-6)*7+1	(X+6)*7	Week X, X=108, 120, …, etc	(X-6)~(X+6)
		Study Day of last dose + 28	> =(Study Day of last dose + 28)		Follow-up	NA
Safety	CSSRS	-63		<-3	Screen	NA
		1	-3	1	Day 1	NA
		15	2	21	Week 2	Day 2 ~ Week 3
		X*7+1	(X-2)*7+1	(X+2)*7	Week X, X>=4, In Clinic and Virtual Visit	(X-2) ~(X+2)

Analysis Set / Domain	Parameter (if applicable)	Target (Day)	Analysis Window (Day)		Analysis Timepoint	Window Weeks
			Beginning Timepoint	Ending Timepoint		
		Study Day of last dose + 28	> =(Study Day of last dose + 28)		Follow-up	NA

NOTES:

1. For safety endpoints and some other results collected for virtual visits, please refer to protocol Section 1.3 SOA for details.

14.4. Appendix 4: Study Phases and Treatment Emergent Adverse Events

14.4.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to Insert Study Specific Text Here

14.4.1.1. Study Phase for Laboratory, HIV Associated Conditions, 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 + 5 days
Post-Treatment	Date > Study Treatment Stop Date + 5 days

14.4.1.2. Study Phase for Adverse Events and Exposure

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

14.4.1.3. Study Phases for Concomitant Medication

- Prior medications: Those taken (i.e., started) before the start date of investigational product.
- Concomitant medications: Those taken (i.e., started or continued) at any time between the start date and stop date of study treatment, inclusive. Prior medications that were continued during this period are also considered as concomitant medications.
- Post treatment medications: Those started after the stop date of study treatment. 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. For any medication starting on the same date as study treatment, it will be assumed that the medication was taken after the subject started taking study treatment.

NOTES:

Please refer to Appendix 7: 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.

14.4.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date + 5 days. • For AE happened in subjects with more than one treatment, AE is assigned to the most recent treatment to the AE start date.

NOTES:

- If the study treatment stop date is missing, then the AE will be considered to be On-Treatment.
- Time of study treatment dosing and start/stop time of AEs should be considered, if collected.

14.5. Appendix 5: Data Display Standards & Handling Conventions

14.5.1. Reporting Process

Software	
• The currently supported versions of SAS software Insert Other Software as Required will be used.	
Reporting Area	
HARP Server	: \us1salx00259
HARP Compound	: \arprod\gsk3640254\mid208379\Reporting effort number
Analysis Datasets	
• Analysis datasets will be created according to Legacy GSK A&R dataset standards OR CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 2.1. If the Study Data Standardization Plan (SDSP) exists for a study, ensure the CDISC versions are consistent.	
Generation of RTF Files	
• RTF files will be generated for all reporting efforts.	

14.5.2. 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://myteams.gsk.com/sites/IDSLLibrary/Lists/DataStandard/DispDataStandard.aspx?ID=30154&Source=/sites/IDSLLibrary/SitePages/DataStdCoreStdByDataGroup.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
• 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

• GSK Statistical Display Principles (4.24) 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.
  • For Insert Endpoint / Parameter the following DP's places will be applied:
  • Summary Statistics:
  • Listings:

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 5.5).
  • Unscheduled or unplanned readings will be presented within the participant's listings.

Unscheduled Visits
• Unscheduled visits will be assigned to a study visit using the all-inclusive windows defined in Section 14.3. • However, data summaries will only report the visits according to the window rules defined in Appendix 3. • Assessments at unscheduled visits will be included for 'any time On-treatment' time points and in data listings, as well any algorithms that make use of additional data (e.g., Snapshot).

Descriptive Summary Statistics	
Continuous Data	Refer to GSK Standard Statistical Display Principal 6
Categorical Data	N, n, frequency, %

Graphical Displays
• Refer to GSK Standard Statistical Display Principals 7.1 to 7.13. • Insert as Required: If any publication related displays have been specified, please provide relevant details

14.5.3. 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. Note: Concentration values will be imputed as per GUI_51487
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: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.
NONMEM/Pop PK File	Pop-PK file (CSV format) for the POP-PK analysis by Clinical Pharmacology Modelling and Simulation function will be created according to the data specification detailed in separate RAP
NONMEM/PK/PD File	PK/PD file (CSV format) for the PK/PD analysis by Clinical Pharmacology Modelling and Simulation function will be created according to the data specification detailed in separate RAP.

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 noted as NC (non-calculable) for the PKPar file and excluded (set to missing) from the PK parameter summary statistics. Refer to PK One document (Standards for the Transfer and Reporting of PK Data using HARP) for handling of non-numeric values in the parameter data.
Descriptive Summary Statistics, Graphical Displays and Listings	If any PK parameter is not calculable because of NQs, it will be noted as NC (non-calculable) for the PKPar file and excluded (set to missing) from the PK parameter summary statistics. Refer to PK One document (Standards for the Transfer and Reporting of PK Data using HARP) for handling of non-numeric values in the parameter data.

14.6. Appendix 6: Derived and Transformed Data

14.6.1. General

Multiple Measurements at One Analysis Time Point
• If there are multiple assessments within Screening window, the last assessment before Day 1 will be used • If there are multiple assessments within Day 1 window, the latest pre-dose assessment will be used • With the exception of the Snapshot endpoints, if after window assignment (see Section 14.3), there are multiple valid assessments of a parameter within the same window, then the following hierarchy will be used to determine the value to be used for summary statistics of observed values: • the assessment closest to the window target Study Day; • if there are multiple assessments equidistant from the target Study Day, then for continuous variables the mean of these values will be used and for categorical variables the worse assessment. For HIV-1 RNA, the geometric mean of the number of copies will be used as opposed to the arithmetic mean • Assessments not chosen for use in summary statistics by this algorithm will still appear in the associated listings. Also, such valid assessments will be used when determining values of potential clinical concern for the 'any time On-treatment' time point, and for any algorithm that has specific rules for which observation to use (e.g., SNAPSHOT). •
Study Day

• Calculated as the number of days from First Dose Date:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < First Dose Date → Study Day = Ref Date – First Dose Date
  • Ref Data ≥ First Dose Date → Study Day = Ref Date – (First Dose Date) + 1

14.6.2. Study Population

Treatment Compliance
• Treatment compliance will be calculated based on the formula: **Treatment Compliance = Number of Actual Doses*100 / (Planned Treatment Duration in Days * Frequency)** • Frequency is 2 for BID and 1 for QD. Treatment compliance could be greater than 100% if there are events of overdose. Cumulative compliance (since Day 1) at each visit will be calculated. • Planned treatment duration will be defined according to the endpoint analyzed.

Endpoint	**Planned Treatment Duration**
Week 24 Snapshot (Primary)	24 weeks
Week 48 Snapshot (Secondary)	48 weeks

Treatment Compliance

- For the final end of study treatment reporting effort, Planned Treatment Duration is defined as 48 weeks for participants on the DTG reference arm. Participants on a GSK3640254 arm who continue to derive benefit will remain on the study until they are transitioned onto a local access program.

Extent of Exposure

- Number of days of on treatment will be calculated based on the formula:
  Duration of Treatment in Days = Treatment Stop Date – (Treatment Start Date) + 1
  This information will also be categorized as: < 12 weeks, 12 to 24 weeks, >24 weeks to 48 weeks, > 48 weeks to 108 weeks, > 108 weeks
- Number of days of exposure to study drug will be calculated based on the formula:
  Duration of Exposure in Days = Sum of Number of Days on Dose
  This information will also be categorized as: < 12 weeks, 12 to 24 weeks, >24 weeks to 48 weeks, > 48 weeks to 108 weeks, > 108 weeks
- Participants who were randomized but did not report a treatment start date will be categorised as having zero days of exposure.
- If there are any treatment breaks during the study, exposure data will be adjusted accordingly.

Demographics

Age

- GSK Statistical Display Standard algorithms will be used for calculating age where birth date will be imputed as follows:
  - For all subjects, the missing date and month will have this imputed as '30th June'.
- Birth date will be presented in listings as 'YYYY'.
- Completely missing dates of birth will remain as missing, with no imputation applied. Consequently, the age of the subject will not be calculated and will remain missing.

14.6.3. Efficacy

HIV-1 RNA

Snapshot

- It is intended to be primarily a virologic assessment of the endpoint, and as such follows a "virology first" hierarchy.
- Plasma HIV1-RNA < 50 c/mL or plasma HIV1-RNA ≥ 50 c/mL within an analysis window is typically determined by the last available plasma HIV-1 RNA measurement in that window while the subject is On-treatment.
- When no HIV-1 RNA data is available within a window, a subject cannot be classified under HIV1-RNA < 50 c/mL. Depending on the reason for lack of data,

HIV-1 RNA
the subject will be classified as a HIV1-RNA ≥ 50 c/mL or reported as 'No Virologic Data at Week X'; in the latter case, the algorithm further classifies the nature of the missing data. Typically, a subject withdrawn (i) due to AE or, (ii) for another reason yet was suppressed at the time, will be counted as 'No Virologic Data at Week X'. Should a subject withdraw for reasons other than AE and was not suppressed at the time, they will be a HIV1-RNA ≥ 50 c/mL. • For each scheduled assessment time, the snapshot response rate for a given threshold (e.g., <50 c/mL) is defined as: $\text{Snapshot Rate} = \frac{\text{Number of responders in that analysis window}}{\text{Number of subjects in the analysis population}}$ • Full details of the algorithm, including the handling of special cases, are included in Section 14.6.3.1 of note, the date at which the subject 'discontinue/withdrawn from the study' in the Snapshot algorithm is the date of treatment discontinuation, rather than the date of study withdrawal,
Plasma HIV-1 RNA
• For summaries and analyses which use HIV-1 RNA level as a continuous measure, the logarithm to base 10 of the value will be used. • HIV-1 RNA results may be provided as censored values, such as <40 or >9,999,999 c/mL. For the purposes of summary statistics, such values will be replaced by the next value beyond the limit of detection, e.g., 39 or 10,000,000 c/mL, respectively, for the given examples. Data listings will show the censored values as provided. • Qualitive measures (i.e. "target detected" and "target non-detected") may also be provided by the laboratory vendor for values <40 c/ml. When a measurement of plasma HIV-1 RNA is below the limit of quantification (i.e. 40 c/mL) and is qualitatively observable that will be denoted as a "Target Detected" measure, while HIV-1 RNA below the limit of quantification that is not qualitatively observable that will be denoted as "Target Not Detected". Any measurements <40 c/mL characterised as "Target Non-Detected" or "Target Detected" will be captured in the database.
CDC HIV-1 Classification and HIV-associated conditions
• HIV associated conditions will be assessed according to the 2014 CDC Revised Classification System for HIV Infection in Adults (see protocol Section 10.10). • Any 'other' conditions reported in the eCRFs will be identified programmatically before being sent for clinical review to determine whether they should be classed as stage 3 associated conditions. Review will be ongoing and as a minimum will take place prior to each reporting effort.

14.6.3.1. Snapshot Algorithm Details

- Consider an analysis visit window, Week X (e.g., Week4, …Week 24, ..Week 48 etc.). The Window for Week X visit is defined in Section 14.3.1. e.g. Week 48 (+/- 6 Week: 295 ≤ Study Day ≤ 378)

- Consider an HIV1-RNA threshold (e.g. 40, 50, 200 copies/mL …) for a given analysis. Our study will use 50 copies/mL as threshold.
- For example: The analysis window 'Week48' and HIV1-RNA threshold of '50 copies/mL' are used for the purposes of illustration. A participant's Snapshot response and reason at Week48 are categorized as below.
    - o HIV1-RNA < 50 copies/mL
    - o HIV1-RNA >= 50 copies/mL

      Data in window not below 50

      Discontinued for lack of efficacy

      Discontinued for other reason while not below 50

      Change in background therapy*
    - o No Virologic Data at Week48 Window

      Discontinued study due to AE or death

      Discontinued study for other reasons

      On study but missing data in window

*All changes are considered non-permitted except a one-time switch to the other option of the NRTI background prior to Week 2 for reasons of tolerability/toxicity.

- The steps in determining response and reasons are indicated in Table below, in the order stated.

Detailed steps

Please note that the following scenarios will NOT be penalized Per Snapshot algorithm (i.e. please exclude these scenarios from **Condition** 1-4).

- Dose reduction, dropping a component, or change in formulation (e.g. 'Tivicay + Kivexa' to 'Triumeq' with the identical ingredients)
- Permitted Change in ART where date of change or date of decision to make permitted change (whichever is earlier) occurs prior to/on the first on-treatment viral load result

Condition (Note that: "Week XX" indicates Week XX window. Week48 is used as an example below)	**Response**	**Reasons**
1. If ***non-permitted*** change in background therapy ***prior to*** Week48	HIV1-RNA ≥ 50	Change in background therapy
2. If ***permitted*** change in background therapy ***prior to*** Week48 AND the latest on-treatment VL prior to/on the date of change is ≥ 50 c/mL [a]	HIV1-RNA ≥ 50	Change in background therapy
3. If ***non-permitted*** change in background therapy ***during*** Week48		
3.1 Last on-treatment VL during Week48 prior to/on the date of change ≥ 50 c/mL	HIV1-RNA ≥ 50	Data in window not below 50
3.2 Last on-treatment VL during Week48 prior to/on the date of change <50 c/mL	HIV1-RNA < 50	
3.3 No VL during Week48 prior to/on the date of change	HIV1-RNA ≥ 50	Change in background therapy
4. If ***permitted*** change in background therapy ***during*** Week48 AND the last on-treatment VL prior to/on the date of change is ≥ 50 c/mL [a]		
4.1 This last on-treatment VL occurs prior to Week48	HIV1-RNA ≥ 50	Change in background therapy
4. 2 This last on-treatment VL occurs during Week48 but prior to/on the date of change	HIV1-RNA ≥ 50	Data in window not below 50
5. If none of the above conditions met		
5.1 VL available during Week48		
5.1.1 Last on-treatment VL duringWeek48 ≥ 50 c/mL	HIV1-RNA ≥ 50	Data in window not below 50
5.1.2 Last on-treatment VL during Week48 <50 c/mL	HIV1-RNA < 50	
5.2 No VL during Week48		
5.2.1 If participants still on study (i.e. The on-treatment period continues beyond the upper bound of Week48 window. For example, for oral treatment, a participant with IP stop date+1> Day 378 of the upper	No virologic data at Week48 Window	On study but missing data in window

Condition (Note that: "Week XX" indicates Week XX window. Week48 is used as an example below)	Response	Reasons
bound of Week48 window, would be considered 'on study' for Week48 snapshot assessment)		
5.2.2 If participants withdraw before/during Week48 due to :		
5.2.2.1 Safety reasons (e.g. AE/death, liver chemistry stopping criteria, renal toxicity withdrawal criteria, QTc withdrawal criteria, as recorded in eCRF Conclusion form)	No virologic data at Week48 Window	Disc. due to AE/death
5.2.2.2 Non-safety related reasons (e.g. Lack of efficacy, protocol deviation, withdrew consent, loss to follow-up, study closed/terminated, investigator discretion et al, as recorded in eCRF Conclusion Form)		
5.2.2.2.1 Last on-treatment VL <50 c/mL OR no on-treatment VL available during study	No virologic Data at Week48 Window	Disc. for other reasons
5.2.2.2.2 Last on-treatment VL ≥ 50 c/mL AND withdrawal due to Lack of efficacy	HIV1-RNA ≥ 50	Disc. for lack of efficacy
5.2.2.2.3 Last on-treatment VL ≥ 50 c/mL AND withdrawal due to all other non-safety related reasons	HIV1-RNA ≥ 50	Disc. for other reason while not below 50

[a]: Excluding permitted change in background therapy where change or decision to change is made prior to/on the first on-treatment viral result

A dataset will be created based on the Snapshot algorithm, where the dataset contains the following information, as a minimum:

- Study identification
- Participant identification
- Study day and date of last blinded treatment
- Virologic outcome based on the snapshot approach (i.e., HIV-1 RNA below 50 copies/mL (c/mL), HIV-1 RNA equal to or above 50 copies/mL, discontinued due to AE or death, discontinued for other reasons, on study but missing data during window)

- The HIV-1 RNA measurement and the corresponding study day and date used to determine the above virologic outcome if the measurement was not missing

- Study day and date when the participant switched to open-label treatment due to lack or loss of virologic suppression, if applicable

- Discontinuation study day and date, reason for discontinuation, and last blinded treatment measurement before discontinuation for participants who discontinued study drug

14.6.4. Virology

PDVF

PDVF is defined as any of the following (and confirmed by a repeat and consecutive plasma HIV-1 RNA measurement between two and four weeks (approx.) after the initial suspected virologic failure sample):

Virologic Non-response

1. Decrease from Baseline (Day 1) in plasma HIV-1 RNA of <1.0 log10 c/mL unless plasma HIV-1 RNA is <200 c/mL by Week 12;
    - **a. SVF**: If there is a decrease < 1 log10 from Baseline at Week 12 and HIV-1 RNA >=200 c/mL, then -> Suspected Virologic Failure
    - **b. PDVF:** If there is a confirmatory sample after 1a, then check if there is a decrease <1 log10 from Baseline and the HIV-1 RNA >=200 c/mL then -> Protocol Defined Virologic Failure

   Note: In addition, subjects having SVF who discontinued at week 12 or have no Viral load after week 12, those subjects would be considered PDVF.

2. Confirmed plasma HIV-1 RNA levels ≥200 c/mL at or after Week 24.
    - **c. SVF:** If a patient has a sample on/after Week 24 and the result is >=200 c/mL then -> Suspected Virologic Failure
    - **d. PDVF:** If after 2c, a patient then has a 2nd consecutive sample >=200 c/mL on/after Week 24 then -> Protocol Defined Virologic Failure.
3. Plasma HIV-1 RNA ≥50 c/mL on repeat testing of Week 24 results and prior to Week 28.
    - e. **SVF**: If a patient has a sample at Week 24 and the result is >=50 c/mL then -> Suspected Virologic Failure
    - f. **PDVF**: If after 3e, a patient then has repeat (retest) sample prior to Week 28 then -> Protocol Defined Virologic Failure.
4. **Virologic Non-response: If a subject met criteria 1b or 2d or 3f then -> PDVF (Virologic Non-response)**

Virologic Rebound

5. Confirmed plasma HIV-1 RNA ≥200 c/mL after confirmed consecutive plasma HIV-1 RNA <50 c/mL.
    - Patient must have 2 consecutive values <50 c/mL, followed at any time (not necessarily immediately) by 2 consecutive values >=200 c/mL
    - g. **SVF**: If a patient has two consecutive samples <50 c/mL, if any following value is >=200 c/mL then -> Suspected Virologic Failure
    - h. **PDVF**: If after 5g, a patient then has a 2nd consecutive sample >=200 c/mL then -> Protocol Defined Virologic Failure.
6. **Virologic Rebound: If a subject met criteria 5h then -> PDVF (Virologic Rebound)**

Genotype

General considerations

- Nominal and analysis window will be included in the listings.
- For summary purposes analysis window will be used.
- Note: Resistance testing will be performed on samples collected at the SVW timepoint (i.e. the timepoint of the initial HIV-1 RNA result which meets one of the Virologic Withdrawal criteria and will be subsequently confirmed in a repeat HIV-1 RNA test. The SVW timepoint is noted as the PDVF timepoint in listings and summaries.

Amino Acid Changes

- A mutation is considered present whenever the encoded amino acid residue differs from the amino acid that would have been encoded by the wild-type (e.g., HXB2, NL43) comparator gene; e.g., Q148K.
- If the encoded amino acid is seen as a mixture of wild-type and mutant amino acid, e.g., Q148Q/K, the mutated amino acid is considered present at the codon of interest.
- If the encoded amino acid is seen as a mixture of two or more amino acids, which may or may not include wild type, e.g., Q184K/H or Q184K/H/Q, etc., for the purposes of calculating the number of mutated amino acids, only one mutation is considered to be present at the codon of interest.
- Treatment emergent mutations: need to meet below three criteria:
  1. New mutation: observed during treatment comparing to baseline at the same codon with the class/region.
  2. Mutations are based on prespecified lists usually identified in the RAP.
     a. Integrase: may use a list generated by Virology that may include non-IAS guidance mutations derived using the Stanford database (e.g., mutations with penalty score >=15; https://hivdb.stanford.edu/dr-summary/mut-scores/INSTI/), or other reliable sources. Note the list may change over time. Usually the major mutations are the ones with evidence of strong resistance to the ART drug.
     b. All other classes: defined by the International Antiviral Society-USA (IAS-USA).
  3. ART Drug class related: based on the class of the ART the subjects are taking during the treatment and the new major mutation within that class will be considered.

Representation of Amino Acid Changes

Mutations	Amino acid change
T69S	Single mutation from amino acid 'T' (vendor reference) to 'S' (sample) at codon '69'
Q148H/K/R	Mixture of amino acid mutations ‘H’, ‘K’ and ‘R’ (sample) from amino acid ‘Q’ (vendor reference) at codon ‘148’
69_1T	First insertion of amino acid 'T' (sample) at codon '69'
69_2S	Second insertion of amino acid 'S' (sample) at codon '69'

_69_3S/A	Third insertion of a mixture of amino acids 'S' and 'A' (sample) at codon '69'
L74L/-	Mixture of amino acid 'L' (sample) and a deletion at codon '74'
V75-	Single deletion of amino acid (sample) at codon '75'

Prespecified Lists – Resistance Associated Mutations

- Summaries and listings of resistance associated mutations in the Integrase Strand Transfer Inhibitor (INSTI) class will use the following pre-defined INSTI list of mutations associated with the development of resistance to BIC, RAL, EVG or DTG.

Category	Mutations
Pre-defined INSTI mutations	H51Y, **T66A/I/K**, L74M, **E92Q/V**/G, Q95K, T97A, G118R, **F121Y**, E138A/K, G140A/C/S, **Y143C/H/R/K/S/G/A, P145S**, **Q146P**, **S147G**, **Q148**N/**H/K/R**, **V151**I/**L**/A, S153F/Y, **N155H**/S/T, E157Q, G163R/K, S230R, R263K, L68V/I*, L74I*, E138T*, G193E*

NOTES:

- Current list includes INSTI mutations identified via the Stanford HIV Resistance database, or identified during in vitro passage of DTG, or as seen in previous DTG studies in INSTI-experienced subjects (i.e. ING112574) and may be modified in case of additional substantive data availability.
- INSTI mutations in bold have the maximum score of 60 and are for any INSTI drug in the Stanford database v9.1 (https://hivdb.stanford.edu/dr-summary/mut-scores/INSTI/,last updated on 2022-06-02); the rest have a maximum score <60.

1. Major resistance mutations to other classes (i.e., NRTI, NNRTI, PI) as defined by the International Antiviral Society-USA (IAS-USA). The most up to date IAS-USA guidelines available at the time of DBF will be used in the analysis. Note that NRTIs A62V, V75I, F77L, and F116Y all need to be present together with Q151M to be resistant, so are not major mutations alone.

Class	Mutations
NRTIs	M41L, K65R/E/N, D67N, K70E/R, L74V, Y115F, M184V/I, L210W, T215Y/F, K219Q/E; [A62V, V75I, F77L, F116Y, Q151M]
NNRTIs	L100I, K101E/P, K103N/S, V106A/M, V108I, E138/A/G/K/Q/R, V179L, Y181C/I/V, Y188C/L/H, G190S/A, H221Y, P225H, F227C, M230I
PIs	D30N,V32I , M46I/L, I47A/V, G48V, I50V/L, I54M/L/V, Q58E, T74P, L76V,V82A/T/F/L/S, N83D, I84V, N88S, L90M

2. Note: 2017 Drug Resistance Mutations Update Volume 24, Issue 4, December 2016/January 2017

Phenotype
Fold change (FC) in IC50 (concentration of drug required to inhibit the sample virus to 50% of its maximum) relative to wild-type control virus is reported from the assays. i.e., FC of sample virus = IC50 of sample virus/IC50 of control virus. Summary statistics for FC will be reported at Baseline and at the PDVF timepoint (time of suspected failure, that was subsequently confirmed) for subjects meeting PDVF criteria. Fold change ratio (Fold change at the time of PDVF/baseline Fold change) will also be summarised.

14.6.5. Safety

ECG Parameters

RR Interval

- IF RR interval (msec) is not provided directly, then RR can be derived as:
  [1] If QTcB is machine read & QTcF is not provided, then:

$$RR = \left[\left(\frac{QT}{QTcB}\right)^2\right] * 1000$$

  [2] If QTcF is machine read and QTcB is not provided, then:

$$RR = \left[\left(\frac{QT}{QTcF}\right)^3\right] * 1000$$

- If ECGs are manually read, the RR value preceding the measurement QT interval should be a collected value THEN do not derive.

Corrected QT Intervals

- When not entered directly in the eCRF, corrected QT intervals by Fredericia's (QTcF) formula will be calculated, in msec, depending on the availability of other measurements.
- IF RR interval (msec) is provided then missing QTcF and/or QTcB will be derived as:

$$QTcF = \frac{QT}{\sqrt[3]{\frac{RR}{1000}}}$$

$$QTcB = \frac{QT}{\sqrt{\frac{RR}{1000}}}$$

Category of QTc Values

Absolute QTc Value	<=450
	451-480
	481-500
	>=501
Increase in QTc Values	Increase of <=30 msec
	Increase of 31-60 msec
	Increase of >60 msec

Adverse Events

AE Severity – DAIDS Grading

- The DAIDS grading (VERSION 2.1, March 2017) for severity of clinical adverse events will be performed.
- See protocol for DAIDS grading criteria.

Adverse Events of Special Interest (AESI)

The preferred terms for each AESI will be review by safety and clinical team and updated before each formal analysis in a separate document. The following table below shows the AESI categories.

AESI

- QT prolongation
- GI intolerability/toxicity
- Psychiatric Events
    - Suicidal ideation/behavior
    - Depression
    - Bipolar Disorder
    - Psychosis
    - Anxiety
    - Sleep Disorders
- Nervous System Disorders
- Skin and subcutaneous tissue disorders

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 smallest unit of one more significant digit than the number of significant digits in the observed values will be added or subtracted (whichever is applicable) in order to impute the corresponding number. For example:
    - Example 1: 2 significant digits (as in "<2.2") will be imputed as 2.19
    - Example 2: 1 significant digit (as in ">5") will be imputed as 5.1
    - Example 3: 0 significant digits (as in "<0") will be imputed as -1".
- There will be no imputation in the data listings; all values will be displayed as recorded in the database.

Lab Toxicities – DAIDS Grading

- Toxicities will be based on the Division of AIDS (DAIDS) grading system, as specified in the protocol.
- Toxicity grades provided by the central laboratory do not distinguish between abnormally high or low criteria, when both are relevant for a particular parameter.
- When summarising toxicity grades for such parameters, they will be categorised as to whether they are above or below the midpoint of normal range.

Parameter	Below Midpoint	Above Midpoint
Calcium	Hypocalcaemia	Hypercalcaemia
Fasted glucose	Hypoglycaemia	Hyperglycaemia
Sodium	Hyponatremia	Hypernatremia
Potassium	Hypokalemia	Hyperkalemia

CCI [redacted]

- CCI [redacted] = (fasting plasma insulin (mU/L) * fasting plasma glucose (mmol/L)) / 22.5.
- CCI [redacted] categories will be categorised as follows:
  - <2
  - 2 to <3
  - 3 to <4
  - >=4

All CCI [redacted] analyses will be based on fasting values and only patients with post-baseline values will be included in analyses (i.e. patients with missing post-baseline CCI [redacted] will not be included in summary tables or figures). Additionally, patients who are diabetic as captured on the medical history form at screening will be excluded from all CCI [redacted] analyses. Finally, any patient who has taken an anti-diabetic medication (ATC code "A10" (**DRUGS USED IN DIABETES**)) as captured on the medical history form up to screening will be removed from the analysis.

Glomerular Filtration Rate (GFR)

- Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [Levey et al.] will be used by the central laboratory to provide an estimate of GFR, in mL/min per 1.73 m2, as follows for the CKD-EPI creatinine equation:

$$GFR = 141 \times \min\left(\frac{CRT_{mg/dL}}{\kappa}, 1\right)^{\alpha} \times \max\left(\frac{CRT_{mg/dL}}{\kappa}, 1\right)^{-1.209} \times 0.993^{Age} \times [1.018 \text{ if Female}] \times [1.159 \text{ if Black}]$$

where age (in years) is at time of assessment, κ = 0.7 if female or 0.9 if male, α = -0.329 if female and -0.411 if male, min() indicates the minimum of CRT/κ or 1, max() indicates the maximum of CRT/κ or 1, and CRTmg/dL is serum creatinine concentration in mg/dL. The serum creatinine concentration in mg/dL is obtained from GSK standard units of □mol/L as CRTmg/dL =0.0113x CRT□mol/L.

- **Cockcroft-Gault formula:**

eClcr= {((140-age) x weight)/(72 SCr)} x 0.85 if female

where eClcr is expressed in milliliters per minute, age in years, weight in kilograms, and serum creatinine (SCr) in milligrams per deciliter.

CKD-EPI Cystatin C Equation (2012)

The following will be used for the CKD-EPI Cystatin C Equation:

eGFR = 133 x min(Scys/0.8, $1^{)-0.499}$ x max (Scys/0.8, $1)^{-1.328}$ x 0.996^{Age} x 0.932 [if female]

Abbreviations / Units

eGFR (estimated glomerular filtration rate) = mL/min/1.73 m2

Scys (standardized serum cystatin C) = mg/l

min = indicates the minimum of Scys/0.8 or 1

max = indicates the maximum of Scys/0.8 or 1

age = years

Assays

14.7. Appendix 7: Reporting Standards for Missing Data

14.7.1. Premature Withdrawals

Element	Reporting Detail
General	Participant study completion (i.e. as specified in the protocol) was defined as complete if they attend the last on treatment visit at the end of study for participants in the GSK3640254 arm, and at Week48 (for participants in the DTG reference arm). The Follow-Up visit is not required for successful completion of the study. The study will be completed when either the development of GSK3640254 is discontinued or until GSK3640254 is locally approved and commercially available (anticipated to be in the year 2027). Alternatively, this study could be completed at an earlier date and participants would continue in a rollover study that would be anticipated to be complete in 2023 • An in-clinic Follow-Up visit will be conducted 2-4 weeks after the last dose of study medication for participants with ongoing AEs, serious adverse events (SAEs) regardless of attributability, and any laboratory abnormalities that are considered to be AEs or potentially harmful to the participant, at the last on-study visit. Assessments at the Follow-up visit should reflect any ongoing complaints (e.g., blood draws to follow a laboratory abnormality). Withdrawn participants will not be 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 and figures, unless otherwise specified.

14.7.2. 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.

Element	Reporting Detail
Snapshot	• In the Snapshot dataset, subjects without HIV-1 RNA data in the assessment window for the visit of interest (due to missing data or discontinuation of IP prior to the visit window) are classified as either 'HIV-1 RNA ≥50 c/mL') or 'No Virologic Data'. For full details of the Snapshot algorithm see Section 14.6.3
Observed Case (OC)	• This dataset uses only the data that is available at a particular timepoint, with no imputation for missing values.
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.

14.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays. • Where necessary, display macros may impute dates as temporary variables for sorting data in listings only. In addition, partial dates may be imputed for 'slotting' data to study phases (see Section 14.4.1) or for specific analysis purposes as outlined below. • Imputed partial dates will not be used to derive study day, time to onset or duration (e.g., time to onset or duration of adverse events), or elapsed time variables (e.g., time since diagnosis). In addition, imputed dates are not used for deriving the last contact date in overall survival analysis dataset.
Exposure	• If study treatment stop date is missing, then for the purposes of calculating exposure, it will be imputed using the date of last visit or the recorded date of withdrawal/completion whichever is earlier. • Partially Missing Stop Day: Last day of the month or last month of the year will be used, unless this is after the stop date of study treatment or withdrawal date; in this case the earliest of the two dates will be used.
Treatment End Date	• If subject is still on-going at data cut-off date, we assume the subject is still on-treatment, treatment end date will the last visit date.
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:

<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
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<tr><td></td><td>

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.

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:

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 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:

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.

</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
<tr><td></td><td>
<table>
<tr><td></td><td>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>

14.8. Appendix 8: Values of Potential Clinical Importance

14.8.1. 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

14.8.2. 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	bpm	<40	>100

14.9. Appendix 9: Population Pharmacokinetic (PopPK) Analyses

Details will be provided in a separate RAP.

14.10. Appendix 10: Time to Event Details

14.10.1. TRDF Detailed Steps

TRDF Detailed steps		
The steps below are for the derivation of TRDF at specific timepoints when the upper bound of the analysis window is used as a cut-off i.e. for the table only.		
Final step of the derivation is made in following order: [1] When one EVENT (1.2, 2.2, 3.2, 4.2) criterion is satisfied, select. In situations where more than one EVENT criteria satisfied, select the earliest event. If the earliest event date satisfies more than one criteria (e.g. subject had PDVF and discontinuation), select PDVF. [2] When one CENSOR (1.1, 2.1, 3.1, 4.1, 5.x) criterion is satisfied, select. Else in situations where more than one CENSOR criteria satisfied, select the latest censor day. If the latest event date satisfies more than one criteria, apply the ordering below.		
Condition	**Censor Status**	**Event Description/AVAL**
1. Subjects met PDVF event criteria during the randomized period. (Based on derived PDVF confirmed prior to cut-off used for the analysis) Then set **tempAVAL**= Study Day of PDVF		
1.1 PDVF event date is after the upper bound of the analysis visit window i.e tempAVAL > upper bound of the analysis visit window for Week X	CNSR=1	EVNTDESC=Censored due to data cutoff. AVAL=Upper bound of analysis visit window.
1.2 PDVF event date is on or before the upper bound of the analysis visit window	CNSR=0	EVNTDESC=PDVF. AVAL= tempAVAL.

TRDF Detailed steps		
i.e tempAVAL ≤ upper bound of the analysis visit window for Week X		
2. Subjects with study withdrawal due to treatment related adverse events during the randomized period (defined as subjects that have reason for withdrawal =AE on disposition page and that the subject has at least one AE considered both: i) drug related (AEREL=Y) and ii) result in withdrawal from study (AEWD=Y)) Then set **tempAVAL**= Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation [from Exposure and Concomitant ART domains]). Assumption: Study day of permanent treatment discontinuation is included in the definition to account for cases where discontinuation information is recorded later. This is a conservative approach consistent with treatment discontinuation preceding withdrawal.		
2.1 Study withdrawal is after the upper bound of the analysis visit window i.e tempAVAL > upper bound of the analysis visit window	CNSR=1	EVNTDESC=Censored due to data cutoff. AVAL=Upper bound of analysis visit window.
2.2 Study withdrawal is on or before the upper bound of the analysis visit window i.e tempAVAL ≤ upper bound of the analysis visit window	CNSR=0	EVNTDESC=Study Withdrawal Due to Treatment Related AE. AVAL= tempAVAL

TRDF Detailed steps		
3: Subjects met protocol defined stopping criteria during the randomized period., (Based on disposition page) Then set **tempAVAL**=Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation [from Study Treatment or CONART eCRF pages]).		
3.1 Protocol defined stopping criteria were met after the upper bound of the analysis visit window i.e tempAVAL > upper bound of the analysis visit window	CNSR=1	EVNTDESC=Censored due to data cutoff. AVAL=Upper bound of analysis visit window.
3.2 Protocol defined stopping criteria were met on or before the upper bound of the analysis visit window i.e tempAVAL ≤ upper bound of the analysis visit window	CNSR=0	EVNTDESC=Study Withdrawal Due to Protocol Defined Criteria. AVAL=tempAVAL
4: Subjects with study withdrawal due to lack of efficacy during the randomized period. (Based on disposition page)		

TRDF Detailed steps		
Then set **tempAVAL**= Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation [from Study Treatment or CONART eCRF pages])		
4.1 Study withdrawal is after the upper bound of the analysis visit window i.e tempAVAL > upper bound of the analysis visit window	CNSR=1	EVNTDESC=Censored due to data cutoff. AVAL=Upper bound of analysis visit window.
4.2 Study withdrawal is on or before the upper bound of the analysis visit window i.e tempAVAL ≤ upper bound of the analysis visit window	CNSR=0	EVNTDESC=Study Withdrawal Due to Lack of Efficacy AVAL= tempAVAL
If none of the above conditions met		
5: Subjects with study withdrawal for other reasons during the randomized period. (Based on disposition page) Then set **tempAVAL**= Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study day of permanent treatment discontinuation [from Study Treatment eCRF pages])		
5.1 Study withdrawal is after the upper bound of the analysis visit window	CNSR=1	EVNTDESC=Censored due to data cutoff.

TRDF Detailed steps		
i.e tempAVAL > upper bound of the analysis visit window		AVAL=Upper bound of analysis visit window.
5.2 Study withdrawal is on or before the upper bound of the analysis visit window i.e tempAVAL ≤ upper bound of the analysis visit window	CNSR=1	EVNTDESC=Censored due to Study Discontinuation for Other Reasons. AVAL=tempAVAL
6: Subject completed the randomized period of the study. (Based on disposition page)	CNSR=1	EVNTDESC= Censored as completed the Randomized Period. AVAL= Date of end of Treatment Phase
7: Subject is ongoing in the study during the randomized period and have not yet completed the randomized period Assumption: this will only be in cases where the reporting effort/analysis is performed midway through the randomized period	CNSR=1	EVNTDESC= Censored due to data cutoff. AVAL=Upper bound of analysis visit window.

14.10.2. TRDF Detailed Steps for the Kaplan-Meier plot

TRDF Detailed steps		
The steps below are for the derivation of TRDF overall i.e. for the Kaplan-Meier plot only.		
Final step of the derivation is made in following order: [1] When one EVENT (conditions 1-4) criterion is satisfied, select. In situations where more than one EVENT criteria satisfied, select the earliest event. If the earliest event date satisfies more than one criteria (e.g. subject had PDVFand discontinuation), select PDVF. [2] When one CENSOR (conditions 5.x) criterion is satisfied, select. Else in situations where more than one CENSOR criteria satisfied, select the latest censor day. If the latest event date satisfies more than one criteria, apply the ordering below.		
Condition	**Censor Status**	**Event Description/AVAL**
1. Subjects met PDVF event criteria during the randomized period. (Based on derived PDVF confirmed prior to cut-off used for the analysis)	CNSR=0	EVNTDESC=PDVF. AVAL=Study Day of PDVF.
2. Subjects with study withdrawal due to treatment related adverse events during the randomized period (defined as subjects that have reason for withdrawal =AE on disposition page and that the subject has at least one AE considered both: i) drug related (AEREL=Y) and ii) result in withdrawal from study (AEWD=Y))	CNSR=0	EVNTDESC=Study Withdrawal Due to Treatment Related AE. AVAL=Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study Day of permanent treatment discontinuation [from Study Treatment eCRF pages]).
3: Subjects met protocol defined stopping criteria during the randomized	CNSR=0	EVNTDESC=Study Withdrawal Due to Protocol Defined Criteria. AVAL=Earliest of (Day of Study

TRDF Detailed steps		
period., (Based on disposition page)		Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study Day of permanent treatment discontinuation [from Study Treatment eCRF pages]).
4: Subjects with study withdrawal due to lack of efficacy during the randomized period. (Based on disposition page)	CNSR=0	EVNTDESC=Study Withdrawal Due to Lack of Efficacy AVAL= Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study Day of permanent treatment discontinuation [from Study Treatment eCRF pages])
If none of the above conditions met		
5: Subjects with study withdrawal for other reasons on or before the end of randomized period. (Based on disposition page)	CNSR=1	EVNTDESC=Censored due to Study Discontinuation for Other Reasons. AVAL=Earliest of (Day of Study Discontinuation [from Disposition page]), date of Withdrawal Visit [from Study Visit domain], Study Day of permanent treatment discontinuation [from Study Treatment eCRF pages])
6: Subject completed the randomized period of the study. (Based on disposition page)	CNSR=1	EVNTDESC= Censored as completed the Randomized Period. AVAL= Date of completion of randomized study period
7: Subject is ongoing in the study during the randomized period and have not yet completed the randomized period	CNSR=1	EVNTDESC= Ongoing in the Study. AVAL=Last visit date

Notes:
Randomized Period = Randomized Phase
Efficacy visit windows should be used throughout for the upper bound of the analysis visit window
Subjects are considered to have completed the randomized period if they completed the Randomized Phase.

By definition, a subject must be on-treatment for a PDVF to be recorded therefore inclusion of study date of treatment discontinuation in the derivation is not required
EVNTDESC, AVAL & CNSR variables created for the following timepoints:
Week 24 or 48 – for the table analysis
Overall – for the Kaplan-Meier plot

14.10.3. ERDF Detailed Steps

Similar algorithm will be applied for ERDF analyses and Kaplan-Meier figure, where condition 2 and 3 in Section 14.10.1 and Section 14.10.2 will not be considered.

14.11. Appendix 11: Abbreviations & Trademarks

14.11.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DBF	Database Freeze
DBR	Database Release
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
EMA	European Medicines Agency
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
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	Intent-To-Treat
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
PopPK	Population PK
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RAMOS	Randomization & Medication Ordering System
SAC	Statistical Analysis Complete
SDSP	Study Data Standardization Plan

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Abbreviation	Description
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings

14.11.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
Tivicay

Trademarks not owned by the GlaxoSmithKline Group of Companies
NONMEM
SAS
WinNonlin

14.12. Appendix 12: List of Data Displays

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

14.12.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.n	1.1 to 1.n
Efficacy	2.1 to 2.n	2.1 to 2.n
Safety	3.1 to 3.n	3.1 to 3.n
Pharmacokinetic	4.1 to 4.n	4.1 to 4.n
Population Pharmacokinetic (PopPK)	5.1 to 5.n	5.1 to 5.n
Pharmacodynamic and / or Biomarker	6.1 to 6.n	6.1 to 6.n
Pharmacokinetic / Pharmacodynamic	7.1 to 7.n	7.1 to 7.n
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

14.12.2. Mock Example Shell Referencing

Nonstandard specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 13: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Population Pharmacokinetic (PopPK)	POPPK_Fn	POPPK_Tn	POPPK_Ln
Pharmacodynamic and / or Biomarker	PD_Fn	PD_Tn	PD_Ln
Pharmacokinetic / Pharmacodynamic	PKPD_Fn	PKPD_Tn	PK/PD_Ln

NOTES:

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

14.12.3. Deliverables

Delivery [Priority] [1]	Description
Week 24/ Week48/EoS	End of study reporting.

NOTES:

1. Indicates priority (i.e. order) in which displays will be generated for the reporting effort

14.12.4. 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 Status and Subject Disposition for the Study Conclusion Record	ICH E3, FDAAA, EudraCT	WEEK 24/ WEEK 48/EOS
1.2.	ITT-E	SD1	Summary of Treatment Sitatus and Reasons for Discontinuation of Study Treatment	ICH E3	WEEK 24/ WEEK 48/EOS
1.3.	ITT-E	ES4	Summary of Subject Disposition at Each Study Epoch	ICH E3	WEEK 24/ WEEK 48
1.4.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements	WEEK 24/ WEEK 48
1.5.	Randomized	NS1	Summary of Number of Subjects by Country and Site ID	EudraCT/Clinical Operations	WEEK 24/ WEEK 48
Protocol Deviation					
1.6.	ITT-E	DV1	Summary of Important Protocol Deviations	ICH E3	WEEK 24/ WEEK 48/EOS,

Study Population Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Population Analysed					
1.7.	Screened	SP1	Summary of Study Populations	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
1.8.	ITT-E	SP2	Summary of Exclusions from the Per Protocol Population	GSK Statistical Display Standard	WEEK 24/ WEEK 48
Demographic and Baseline Characteristics					
1.9.	ITT-E	DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	WEEK 24/ WEEK 48
1.10.	Screened	DM11	Summary of Age Ranges	EudraCT	WEEK 24/ WEEK 48
1.11.	ITT-E	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	WEEK 24/ WEEK 48
Prior and Concomitant Medications					
1.12.	ITT-E	MH1 / MH4	Summary of Current/Past Medical Conditions	ICH E3	WEEK 24/ WEEK 48/EOS
1.13.	ITT-E	CM1	Summary of Concomitant Medications	ICH E3	WEEK 24/ WEEK 48/EOS

Study Population Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
				See GSK Statistical Display Standard	
Exposure and Treatment Compliance					
1.14.	ITT-E	EX1	Summary of Exposure to Study Treatment for Daily Dosed Drugs	ICH E3	WEEK 24/ WEEK 48/EOS

14.12.5. Efficacy Tables

Efficacy Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Plasma HIV-RNA < 50					
2.1.	ITT-E	Shell 5	Summary of Posterior Probability of Treatment Difference of Plasma HIV-1 RNA <50 copies/mL at Week 24 - Snapshot		WEEK 24
2.2.	ITT-E	Shell 1.1	Summary of Analysis of Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL at WEEK 48- Snapshot		WEEK 24/ WEEK 48
2.3.					
2.4.	PP	Shell 5	Summary of Posterior Probability of Treatment Difference of Plasma HIV-1 RNA <50 copies/mL at WEEK 48 - Snapshot		WEEK 24
2.5.					
2.6.	PP	Shell 1	Summary of Analysis of Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL at WEEK 48 - Snapshot		WEEK 24/ WEEK 48
2.7.	ITT-E	Shell 1	Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit - Observed		WEEK 24/ WEEK 48/EOS
2.8.	ITT-E	Shell 2	Summary of Study Outcomes (<50 c/mL) at WEEK 48 Snapshot Analysis		WEEK 24/ WEEK 48
2.9.	ITT-E	Shell 1	Summary of Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL at WEEK 48- Snapshot		WEEK 24/ WEEK 48
2.10.	ITT-E	Shell 4	Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit and Subgroups - Snapshot	Only include timepoints up	WEEK 24/ WEEK 48

Efficacy Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
				to Week 24	
2.11.	PP	Shell 2	Summary of Study Outcomes (<50 c/mL) at WEEK 48 Snapshot Analysis		WEEK 24/ WEEK 48
2.12.	ITT-E	Shell 4	Percent of Subjects with Plasma HIV-1 RNA <50c/mL at WEEK 48 By Subgroups- Snapshot Analysis		WEEK 24/ WEEK 48
2.13.					
PDVF					
2.14.	ITT-E	GSK35158 64 Table 2.18 mid204861 /Primary 1	Cumulative Proportion of Subjects Meeting PDVF by Visit by Type of Criteria		WEEK 24/ WEEK 48/EOS
2.15.	ITT-E	table 2.19 mid204861 /Primary 1	Distribution of Quantitative Plasma HIV-1 RNA Results at PDVF	Data only for the subjects that meet PDVF.	WEEK 24/ WEEK 48/EOS
Post-baseline HIV-1 Disease Progression					
2.16.	ITT-E	Table 2.24 mid204861 /Primary 1	Summary of Post-Baseline HIV-1 Associated Conditions Including Recurrences		WEEK 24/ WEEK 48/EOS
2.17.	ITT-E	Table 2.25	Summary of Post-Baseline HIV-1 Associated Conditions		WEEK 24/

Efficacy Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
		mid204861 /Primary 1	Excluding Recurrences		WEEK 48/EOS
2.18.	ITT-E	Table 2.26 mid204861 /Primary 1	Summary of Post-Baseline HIV-1 Disease Progressions		WEEK 24/ WEEK 48/EOS
Change from Baseline in Log10 HIV-1 RNA and CD4					
2.19.	ITT-E	LB1	Summary of Change from Baseline in Log Plasma HIV-1 RNA by Visit		WEEK 24/ WEEK 48/EOS
2.20.	ITT-E	LB1	Summary of Change from Baseline in CD4+ TCell Count (cells/mm^3) by Visit		WEEK 24/ WEEK 48/EOS
2.21.	ITT-E	LB1	Summary of Change from Baseline in in CD4+/CD8+ count ratio by Visit		WEEK 24/ WEEK 48/EOS
Kaplan – Meier					
2.22.	ITT-E	Shell 7	Summary of Kaplan-Meier Estimates of Proportion of Subjects Without PDVF at WEEK 48 - Treatment Related Discontinuation = Failure	Refer to: GSK3515864/ 208090/primary_01 Table 2.24	WEEK 24/ WEEK 48
2.23.	ITT	Shell 7	Summary of Kaplan-Meier Estimates of Proportion of Subjects	Refer to:	WEEK 24/

Efficacy Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
	-E		Without PDVFat WEEK 48 - Efficacy Related Discontinuation = Failure	GSK3515864/ 208090/primary_01 Table 2.25	WEEK 48
2.24.	ITT-E	GSK3515864 Table 2.17 mid204861/primary_01	Statistical Analysis of Kaplan-Meier Estimates of Time to Viral Suppression Overall and by Baseline HIV-1 RNA Subgroups	Add categories: Baseline HIV-1 RNA (c/mL) < 100,000 vs. ≥100,000	WEEK 24/ WEEK 48

14.12.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Insert Endpoint Category					
2.1.	ITT-E	Shell 7	Unadjusted Treatment Difference in Proportion (95% CI) of Subjects with HIV-1 RNA <50 c/mL at WEEK 48 by Subgroup - Snapshot Analysis		WEEK 24/ WEEK 48
2.2.	ITT-E	Figure 2.4 mid204861/Primary 1	Kaplan-Meier Plot of Time to Failure - Treatment related discontinuation = Failure (TRDF)		WEEK 24/ WEEK 48
2.3.	ITT-E	Figure 2.5 mid204861/Primary 1	Kaplan-Meier Plot of Time to Failure - Efficacy related discontinuation = Failure (ERDF)		WEEK 24/ WEEK 48
2.4.	ITT-E	Figure 2.6 mid204861/Primary 1	Kaplan-Meier Plot of Time to Viral Suppression Overall and by Baseline HIV-1 RNA Subgroups	categories: Baseline HIV-1 RNA (c/mL) <= 100,000 vs. > 100,000 for WK 48 Time to Viral Suppression means the first time HIVRNA<50 c/mL.	WEEK 24/ WEEK 48

14.12.7. Safety Tables

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	Safety	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3	WEEK 24/ WEEK 48/EOS
3.2.	Safety	AE5B	Summary of All Adverse Events by Maximum Grade / Intensity by System Organ Class and Preferred Term		WEEK 24/ WEEK 48/EOS
3.3.	Safety	AE3	Summary of Common (>=2%) Adverse Events by Overall Frequency	ICH E3	WEEK 24/ WEEK 48/EOS
3.4.	Safety	AE3	Summary of Common (>=2%) Grade 2-4 Adverse Events by Overall Frequency	ICH E3	WEEK 24/ WEEK 48/EOS
3.5.	Safety	AE1	Summary All Drug-Related Adverse Events by System Organ Class and Preferred Term/by Overall Frequency	ICH E3	WEEK 24/ WEEK 48/EOS
3.6.	Safety	AE15	Summary of Common (>=2%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT	WEEK 24/ WEEK 48/EOS

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.7.	Safety	AE3	Summary of Non-Serious Drug-Related Adverse Events by Overall Frequency	Plain Language Summary requirements.	WEEK 24/ WEEK 48/EOS
Serious and Other Significant Adverse Events					
3.8.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT	WEEK 24/ WEEK 48/EOS
3.9.	Safety	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term /by Overall Frequency	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
Laboratory: Chemistry					
3.10.	Safety	LB1	Summary of Chemistry Changes from Baseline	ICH E3	WEEK 24/ WEEK 48/EOS
3.11.	Safety	LB16	Summary of Worst Case Chemistry Results by Maximum Grade Increase at Post-Baseline Relative to Baseline	ICH E3	WEEK 24/ WEEK 48/EOS
Laboratory: Haematology					
3.12.	Safety	LB1	Summary of Hematology Changes from Baseline	ICH E3	WEEK 24/ WEEK 48/EOS

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.13.	Safety	LB16	Summary of Worst Case Hematology Results by Maximum Grade Increase at Post-Baseline Relative to Baseline	ICH E3	WEEK 24/ WEEK 48/EOS
Laboratory: Urinalysis					
3.14.	Safety	UR1	Summary of Worst Case Urinalysis Results (Discrete or Character Values) Post-Baseline Relative to Baseline	ICH E3	WEEK 24/ WEEK 48/EOS
Laboratory: Hepatobiliary (Liver)					
3.15.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
3.16.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
ECG					
3.17.	Safety	EG1	Summary of ECG Findings	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
3.18.	Safety	EG10	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
3.19.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.20.	Safety	EG11	Summary of Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
Vital Signs					
3.21.	Safety	VS1	Summary of Change from Baseline in Vital Signs	ICH E3	WEEK 24/ WEEK 48/EOS
3.22.	Safety	VS3	Summary of Worst Case Vital Signs Results by Post-Baseline Relative to Baseline	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
CSSRS					
3.23.	Safety	CSSRS1	Summary of Subjects with Post Baseline eCSSRS Suicidal Ideation or Behaviour	Only include participants who have suicidal ideation or behaviour	WEEK 24/ WEEK 48/EOS
COVID-19 Related AE					
3.24.	Safety	PAN1A	Summary of COVID-19 Assessment		WEEK 24/ WEEK 48
3.25.	Safety	PAN3A	Summary of COVID-19 Symptoms for Subjects with Adverse Events	Conditional Display	WEEK 24/ WEEK 48
Adverse Events of Special interest					

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.26.	Safety	SAF_T10	Summary of Characteristics of Post Baseline QT prolongation Adverse events of Special interest		WEEK 24/ WEEK 48/EOS
3.27.	Safety	SAF_T10	Summary of Characteristics of Post Baseline Gastrointestinal intolerability/gastric toxicity Adverse events of Special interest		WEEK 24/ WEEK 48/EOS
3.28.	Safety	SAF_T10	Summary of Characteristics of Post Baseline Psychiatric Adverse events of Special interest		WEEK 24/ WEEK 48/EOS
3.29.	Safety	SAF_T10	Summary of Characteristics of Post Baseline Nervous system disorders Adverse events of Special interest		WEEK 24/ WEEK 48/EOS
3.3(	Safety	SAF_T10	Summary of Characteristics of Post Baseline Skin and subcutaneous tissue disorder Adverse events of Special interest		WEEK 24/ WEEK 48/EOS
Biomarkers (Bone, Renal and Inflammatory)					
3.31	Safety	LB1	Summary of Change from Baseline in Bone Biomarkers by Visit		WEEK 24/ WEEK 48
3.32	Safety	LB1	Summary of Change from Baseline in Renal Biomarkers by Visit		WEEK 24/ WEEK 48
3.33	Safety	LB1	Summary of Change from Baseline in Renal Biomarkers by Visit- Loge Transformed Data		WEEK 24/ WEEK 48
3.34	Safety	LB1	Summary of Change from Baseline in Inflammatory Biomarkers - Loge Transformed Data		WEEK 24/ WEEK 48

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.35	Safety	LB1	Summary of Change from Baseline in Stomach/Gastric Biomarkers		WEEK 24/ WEEK 48
3.36	Safety	LB1	Summary of Change from Baseline in [CCI redacted] by Visit - Loge Transformed Data		WEEK 24/ WEEK 48
3.37	Safety	LB1	Summary of Change from Baseline in HbA1c by Visit		WEEK 24/ WEEK 48
3.38	Safety	LB1	Summary of Change from Baseline in Fasting Lipids by Visit	display both mmol/L and mg/DL	WEEK 24/ WEEK 48
3.39	Safety	LB1	Summary of Change from Baseline in Bone Biomarkers by Subgroup and Visit		WEEK 24/ WEEK 48
3.40	Safety	LB1	Summary of Change from Baseline in Renal Biomarkers by Subgroup and Visit		WEEK 24/ WEEK 48
3.41	Safety	LB1	Summary of Change from Baseline in Renal Biomarkers by Subgroup and Visit - Loge Transformed Data		WEEK 24/ WEEK 48
3.42	Safety	LB1	Summary of Change from Baseline in Inflammatory Biomarkers by Subgroup and Visit - Loge Transformed Data		WEEK 24/ WEEK 48
3.43	EGD Sub Study	LB1	Summary of Change from Baseline in Stomach/Gastric Biomarkers Subgroup and Visit		WEEK 24/ WEEK 48

Safety: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.44	Safety	gsk3515864/ mid204862/p rimary_01 T1.27	Summary of Current Cardiovascular System Conditions		WEEK 24/ WEEK 48/EOS
3.45	EGD Sub Study	PRF1	Summary of Gastric Biopsy Findings by Stomach Region and EGD Grading		WEEK 24/EOS
3.46	EGD Sub Study	PRF2	Summary of Treatment Emergent Gastric Biopsy Findings by Stomach Region and EGD Grading		WEEK 24/EOS
3.47	EGD Sub Study	PRF3	Summary of Staining Methods by Visit		WEEK 24/EOS
3.48	EGD Sub Study	EGD1	Summary of Esophagus and Stomach Visualization and Savary-Miller Grades		WEEK 24/EOS
3.49	EGD Sub Study	EGD2	Summary of EGD Findings by Esophagus and Stomach Regions and Location of greatest impact by Grade		WEEK 24/EOS
3.50	EGD Sub Study	EGD3	Summary of Treatment Emergent EGD Findings by Esophagus and Stomach Regions and Location of greatest impact by Grade		WEEK 24/EOS

14.12.8. Safety Figures

Safety: Figures					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
3.1.	Safety	AE10	Plot of Common (>=2%) Adverse Events and Relative Risk / Other Statistics	GSK Statistical Display Standard	WEEK 24/ WEEK 48
Laboratory					
3.2.	Safety	LIVER14	Scatter Plot of Maximum vs. Baseline for ALT	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
3.3.	Safety	LIVER9	Scatter Plot of Maximum ALT vs. Maximum Total Bilirubin	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS

14.12.9. Virology tables

Virology: Tables					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.1.	PDVF	PFG1	Summary of Major Mutations of NRTI, NNRTI and PI Classes at Baseline and Time of PDVF	Template: gsk3515864/mid20486 1/primary_09/table 4.4.	WEEK 24/ WEEK 48/EOS
4.2.	PDVF	VIR_T4	Summary of Phenotypic Susceptibility by Drug and Drug Class at the Time of PDVF for subjects meeting PDVF criteria	Template: gsk3515864/mid20486 1/primary_01/table 4.8.	WEEK 24/ WEEK 48/EOS
4.3.	PDVF	VIR_T6	Summary of Fold Change of IC50 at - Time of PDVF		WEEK 24/ WEEK 48/EOS
4.4.	PDVF	PFG2	Summary of Emergent INSTI Mutations at Time of PDVF	Please follow template from gsk3515864/mid20486 1/primary_01/table 4.3	WEEK 24/ WEEK 48/EOS
4.5.	Geno/Pheno	PFG2	Summary of Emergent NRTI, NNRTI and PI Classes at Time of PDVF		WEEK 24/ WEEK 48/EOS

Note : Please add a footnote in the tables saying the PDVF subjects with Viral load >=400 are considered at PDVF timepoint.

14.12.10. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Intensive PK - PK Concentration Data					
5.1	Intensive PK	PK01	Summary of Plasma GSK3640254 PK Concentration-Time Data by Nominal Time Relative to Dose	Sorted by Study Visit and Time relative to Dose	WEEK 24
Intensive PK Derived Parameters					
5.2	Intensive PK	PK06	Summary of untransformed and $\log_e$-transformed Derived Plasma GSK3640254PK Parameters		WEEK 24
Sparse PK - PK Concentration Data					
5.3	Sparse PK	PK01	Summary of Plasma GSK3640254PK Concentration-Time Data by Visit and Nominal Time Relative to Dose	Sorted by Study Visit and/or Time (window) relative to Dose	WEEK 24/ WEEK 48

14.12.11. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**GSK Standard / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Intensive PK - PK Concentration Data					
5.1.	Intensive PK	PK24	Individual Plasma GSK3640254 Concentration-Time Plots (linear and Semi-log)	Overlay all individual profiles	WEEK 24
5.2.	Intensive PK	PK19	Mean and SD Plasma GSK3640254 Concentration-Time plots (linear and semi-log)		WEEK 24
5.3.	Intensive PK	PK18	Median Plasma GSK3640254 Concentration-Time plots (linear and semi-log)		WEEK 24

14.12.12. 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	WEEK 24/ WEEK 48/EOS
2.	ITT-E	SD2	Listing of Reasons for Study Treatment Discontinuation	ICH E3	WEEK 24/ WEEK 48/EOS
3.	ITT-E	BL1	Listing of Subjects for Whom the Treatment Blind was Broken	ICH E3	WEEK 24/ WEEK 48
4.	Screened	ES7	Listing of Reasons for Screen Failure	CS CORE; add subreason, i.e # of IE criteria	WEEK 24/ WEEK 48
Protocol Deviations					
5.	ITT-E	DV2	Listing of Important Protocol Deviations	ICH E3	WEEK 24/ WEEK 48/EOS
6.	ITT-E	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	WEEK 24/ WEEK 48

ICH: Listings					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Populations Analysed					
7.	ITT-E	SP3	Listing of Subjects Excluded from Any Population	ICH E3 For PP population and ITTES	WEEK 24/ WEEK 48

ICH: Listings					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demographic and Baseline Characteristics					
8.	ITT-E	DM2	Listing of Demographic Characteristics	ICH E3	WEEK 24/ WEEK 48
9.	ITT-E	DM9	Listing of Race	ICH E3	WEEK 24/ WEEK 48
Prior and Concomitant Medications					
10.	ITT-E	CM3	Listing of Concomitant Medications	Based on GSK Drug Dictionary	WEEK 24/ WEEK 48/EOS
Exposure and Treatment Compliance					
11.	Safety	EX3	Listing of Exposure Data	ICH E3	WEEK 24/ WEEK 48/EOS
Adverse Events					
12.	Safety	AE8CP	Listing of All Adverse Events	ICH E3	WEEK 24/ WEEK 48/EOS
13.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	WEEK 24/ WEEK 48/EOS
Serious and Other Significant Adverse Events					

ICH: Listings					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
14.	Safety	AE8CP	Listing of All Drug-related Adverse Events	ICH E3	WEEK 24/ WEEK 48/EOS
15.	Safety	AE8CP	Listing of Serious Adverse Events (Fatal and Non-Fatal)	ICH E3	WEEK 24/ WEEK 48/EOS
16.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	WEEK 24/ WEEK 48/EOS
17.	Safety	AE8CP	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	WEEK 24/ WEEK 48/EOS

ICH: Listings					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
All Laboratory					
18.	Safety	LB5A	Listing of All Laboratory Data for Subjects with Any Value of Toxicity Grade 1 or Above	ICH E3	WEEK 24/ WEEK 48/EOS
19.	Safety	LB5A	Listing of Laboratory Values of Toxicity Grade 1 or Above	ICH E3	WEEK 24/ WEEK 48/EOS
20.	Safety	LB14	Listing of Laboratory Data with Character Results	ICH E3	WEEK 24/ WEEK 48/EOS
21.	Safety	LB5A	Listing of Urinalysis Data for Subjects	ICH E3, The columns related to normal range and flags can be excluded.	WEEK 24/ WEEK 48/EOS

14.12.13. Non-ICH Listings

Non-ICH Listings					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
22.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
Hepatobiliary (Liver)					
23.	Safety	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
ECG					
24.	Safety	EG3	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
25.	Safety	EG3	Listing of ECG Values of Potential Clinical Importance	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
26.	Safety	EG5	Listing of All ECG Findings for Subjects with an Abnormal ECG Finding	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
27.	Safety	EG5	Listing of Abnormal ECG Findings	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
Vital Signs					
28.	Safety	VS4	Listing of All Vital Signs Data for Subjects with Any Value of Potential Clinical Importance	GSK Statistical Display Standard	WEEK 24/ WEEK 48

Non-ICH Listings					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
29.	Safety	VS4	Listing of All Vital Signs Data	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
COVID-19 Related AE					
30.	Safety	PAN12	Listing of COVID-19 Assessments and Symptom Assessment		WEEK 24/ WEEK 48
Other					
31.	Safety	PREG1	Listing of Subjects Who Became Pregnant During the Study	GSK Statistical Display Standard	WEEK 24/ WEEK 48/EOS
32.	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event		WEEK 24/ WEEK 48/EOS
PK Endpoints					
33.	PK	PK07	Listing of GSK3640254 Pharmacokinetic Concentration-Time Data		WEEK 24/ WEEK 48
Efficacy					
34.	ITT-E	VF4	Listing of Plasma HIV-1 RNA data for subjects with PDVF		WEEK 24/ WEEK 48/EOS

Non-ICH Listings					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
35.	ITT-E	gsk3515864/mid208090/primary_01 Listing 10	Listing of Quantitative and Qualitative Plasma HIV-1 RNA Data		WEEK 24/ WEEK 48/EOS
36.	ITT-E	gsk3515864/mid208090/primary_01 Listing 44	Listing of CD4+ Cell Count Data		WEEK 24/ WEEK 48/EOS
37.	ITT-E	gsk3515864/mid208090/primary_01 Listing 45	Listing of CD8+ and CD4+/CD8+ Cell Count Ratio Data		WEEK 24/ WEEK 48/EOS
38.	ITT-E	HIV4	Listing of Stage 3 HIV-1 Associated Conditions		WEEK 24/ WEEK 48/EOS
Virology					

Non-ICH Listings					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
39.	Geno/Pheno	VIR_L1	Listing of All Genotypic Data	Includes IC50 and Fold change. Fold change ratio to be included in the Listing of Genotypic and Phenotypic data in PDVF subjects	WEEK 24/ WEEK 48/EOS
40.	Geno/Pheno	VIR_L1	Listing of All Pheotypic Data	Includes IC50 and Fold change. Fold change ratio to be included in the Listing of Genotypic and Phenotypic data in PDVF subjects	WEEK 24/ WEEK 48/EOS
41.	Safety	gsk3515864/mid204862/primary_01 Listing 62	Listing of Cardiovascular Events		WEEK 24/ WEEK 48/EOS
42.	EGD Sub Study	PRF4	Listing of Gastric Biopsy findings		WEEK 24/EOS

Non-ICH Listings					
No.	**Population**	**GSK Standard/ Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
43.	EGD Sub Study	EGD4	Listing of EGD findings		WEEK 24/EOS

14.13. Appendix 13: Example Mock Shells for Data Displays

Note: All the tables will be presented for the following 4 treatment groups:

- GSK254 100 mg + 2NRTIs
- GSK254 150 mg + 2NRTIs
- GSK254 200 mg + 2NRTIs
- DTG 50 mg + 2NRTIs

Shell 1:

Protocol: 208379 Page 1 of 1
Population: Intent-To-Treat Exposed

Percent of Subjects with Plasma HIV-1 RNA < 50 c/mL by Visit
- Snapshot Analysis

Actual Relative Time	Trt A (N=246)	Trt B (N=247)
Baseline	XX / XX (XX%)	XX / XX (XX%)
Week 4	XX / XX (XX%)	XX / XX (XX%)
Week 12	.	.
Week 24	.	.
Week 36	XX / XX (XX%)	XX / XX (XX%)

Shell 1.1

Protocol: 208379 Page 1 of n

Population: Intent-to-Treat Exposed

Table T_EFF2

Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA < 50 c/mL at Week 24 – Snapshot Analysis

Treatment	N	Number of HIV-1 RNA <50 c/mL/Total Assessed	Percent (95% CI) [1]	Difference in Percent (95% CI) [2]	Adjusted Difference in Percent (95% CI) [3]
Trt. A	XXX	X/XXX (XX%)	(X.X, X.X)	X.X (X.X, X.X)	X.X (X.X, X.X)
Trt. B	XXX	X/XXX (XX%)	(X.X, X.X)	X.X (X.X, X.X)	X.X (X.X, X.X)
Trt. C	XXX	X/XXX (XX%)	(X.X, X.X)	X.X (X.X, X.X)	X.X (X.X, X.X)
Control	XXX	X/XXX (XX%)	(X.X, X.X)		

Note: [1] Confidence Intervals estimated using the Wilson (Score) method
Note: [2] Difference: Proportion on GSK254 + 2 NRTIs - Proportion on DTG + 2 NRTIs
Note: [3] Based on the Cochran-Mantel Haenszel stratified analysis for adjusting the following baseline stratification factors: Screening HIV-1 RNA (<100,000 copies/mL or >=100,000 copies/mL) and Initial background dual NRTI (ABC/3TC or FTC/TAF)

Shell 2:

Protocol: 208379 Page 1 of n

Population: Intent-To-Treat Exposed

Table 2.xx
Summary of Study Outcomes (Plasma HIV-1 RNA >=/< 50 c/mL) at Week X
- Snapshot Analysis

Outcome	Trt A (N=xx)	Trt B (N=xx)
HIV1-RNA < 50 copies/mL	xx (xx%)	xxx (xx%)
HIV1-RNA >= 50 copies/mL	xx (xx%)	xx (xx%)
Data in window and HIV-1 RNA >= 50 copies/mL	xx (xx%)	xx (xx%)
Discontinued for lack of efficacy	xx (xx%)	xx (xx%)
Discontinued for other reason while HIV-1 RNA >= 50 copies/mL	xx (xx%)	xx (xx%)
Change in background therapy	xx (xx%)	xx (xx%)
No Virologic Data at Week X Window	xx (xx%)	xx (xx%)
Discontinued study due to AE or Death	xx (xx%)	xx (xx%)
Discontinued study for Other Reasons	xx (xx%)	xx (xx%)
On study but missing data in window	xx (xx%)	xx (xx%)

Shell 4:

Protocol: 208379 Page 1 of xx

Population: Intent-to-Treat Exposed

Table 2.6

Percent of Subjects with Plasma HIV-1 RNA <threshold c/mL by Visit and Subgroup - Snapshot Analysis

Subgroup		Act. Rel. Time	Trt. A (N=XXX)	Trt. B (N=XXX)
Sex	Female	Baseline	xxx/XXX	xxx/XXX
		Week 2	xxx/XXX	xxx/XXX
		Week 4	xxx/XXX	xxx/XXX
		Week 12	xxx/XXX	xxx/XXX
		...	xxx/XXX	xxx/XXX
		Week 48	xxx/XXX	xxx/XXX
		...	xxx/XXX	xxx/XXX
	Male	Baseline	xxx/XXX	xxx/XXX
		Week 2	xxx/XXX	xxx/XXX
		Week 4	xxx/XXX	xxx/XXX
		Week 12	xxx/XXX	xxx/XXX
		...	xxx/XXX	xxx/XXX
		Week 48	xxx/XXX	xxx/XXX
		...	xxx/XXX	xxx/XXX

Shell 5

Protocol: 208379

Population: Intent-to-Treat Exposed (ITT-E)

Table 2.1

Summary of Posterior Probability of Treatment Difference of Plasma HIV-1 RNA <50 copies/mL at Week 24 - Snapshot

Result	Arm 1 to 3: GSK254 XX mg + 2NRTIs (N=XXX)	Arm 4: DTG 50 mg + 2NRTIs (N=XXX)
Overall		
Number of Subjects	XX	XX
Number (%) with HIV-1 RNA <50 c/mL	XX (XX%)	XX (XX%)
(95% CI) [1]	(XX%, XX%)	(XX%, XX%)
Overall Treatment Difference compared to Arm 4		
% with HIV-1 RNA <50 c/mL	XX%	NE
(95% CI)[3]	(XX%, XX%)	NE
Point Estimate (%) of rate of HIV-1 RNA <50 c/mL [2]		
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
(95% CI)	(XX%, XX%)	(XX%, XX%)
Point Estimate (%) of Treatment Difference [2]		
Mean (SD)	XX.X (XX.XX)	NE
Median	XX.X	NE
(95% CI)	(XX%, XX%)	NE

Posterior Probability P(True difference of Arm 1:3 - Arm 4 >= -10% | data)[4]	0.XXXX	NE

[1] Confidence interval is based on frequentist estimate using Clopper-Pearson.
[2] The point estimate of HIV-1 RNA <50 c/mL and its 95% credible interval are estimated from a Bayesian hierarchical model that incorporates the analysis stratification factors. The posterior distribution of the rate for each arm is derived using a mixture of the posterior distributions of the rate for each stratum with weight proportional to the sample size for each stratum.
[3] Confidence interval of the frequentist estimate of response rate difference is based on Newcombe.
[4] Success with complete data is defined as the posterior probability P(Arm1:3 - Arm 4 >= -10% | data) > 85%
NE = Not estimable

Shell 6

Protocol: 208379

Population: Safety

Table 3.xx
Summary of Characteristics of Adverse Events of Special Interest

Preferred Term: Depression

	Trt. A (N=100)	Trt. B (N=100)
Number of Subjects with Event	xx (xx%)	xx (xx%)
Number of Events	xx	xx
Event Characteristics [1]		
n	xx	xx
Serious	xx (xx%)	xx (xx%)
Drug-related	xx (xx%)	xx (xx%)
Leading to Withdrawal	xx (xx%)	xx (xx%)
Severe/Potentially life threatening or Grade 3/4	xx (xx%)	xx (xx%)
Fatal of Grade 5	xx (xx%)	xx (xx%)
Number of occurences		
n	xx	xx
One	xx (xx%)	xx (xx%)
Two	xx (xx%)	xx (xx%)
Three or more	xx (xx%)	xx (xx%)
Outcome [2]		
n	xx	xx
Recovered/resolved	xx (xx%)	xx (xx%)
Recovering/resolving	xx (xx%)	xx (xx%)
Not recovered/not resolved	xx (xx%)	xx (xx%)
Recovered/resolved with sequalae	xx (xx%)	xx (xx%)
Fatal	xx (xx%)	xx (xx%)
Maximum Grade or Intensity		

N	xx	xx
CCI or Grade 1	xx (xx%)	xx (xx%)
CCI or Grade 2	xx (xx%)	xx (xx%)
CCI or Grade 3	xx (xx%)	xx (xx%)
CCI or Grade 4	xx (xx%)	xx (xx%)
CCI or Grade 5	xx (xx%)	xx (xx%)
Action Taken [3]		
n	xx	xx
Dose Not Changed	xx (xx%)	xx (xx%)
Drug Interrupted	xx (xx%)	xx (xx%)
Drug Withdrawn	xx (xx%)	xx (xx%)
Dose Increased	xx (xx%)	xx (xx%)
Dose Reduced	xx (xx%)	xx (xx%)
Not Applicable	xx (xx%)	xx (xx%)

Note: Division of AIDS (DAIDS) version 2.1, March 2017 is used for severity grading.
Note: AEs are coded using MedDRA vxx.x
Note: [1] Subjects may be included in more than one category for 'Event Characteristics'.
Note: [2] Outcome worst case hierarchy: Fatal > Not Recovered/Not Resolved > Recovered/Resolved with sequelae> Recovering/Resolving > Recovered/Resolved
Note: [3] Subjects are counted once under each action that was taken.
Programming note: Repeat for all AESI:

Shell HIV 4

Protocol:
Population: Intent-to-Treat Exposed

Listing X

Listing of Stage 3 HIV-1 Associated Conditions

Treatment:

Site ID/ Unique Subject ID	Category/ Condition	Actual Treatment State	Start Date/ Days Since 1st Dose	Progression	Previous Condition?
PPD	HIV Infection Stage 3/ Candidiasis, esophageal	On-treatment	PPD /8 3 d	HIV Infection Stage 2 to HIV Infection Stage 3 Event	Yes
PPD	HIV Infection Stage 3/ *DIFFUSE LARGE B CELL NON HODGKIN'S LYMPHOMA	On-treatment	PPD /7 d	HIV Infection Stage 2 to HIV Infection Stage 3 Event	No

Note: *Clinically reviewed and determined to be HIV Infection Stage 3 Event.

Shell 7

Population: Intent-to-Treat Exposed

Table 2.xx
Summary of Kaplan- Meier Estimates of Proportion of Subjects Without Protocol Defined Virologic Failure at Week X - Treatment Related Discontinuation = Failure

	Trt A (N=xXx)	Trt B (N=xxx)
Number of Subjects		
Protocol Defined Virologic Failure or discontinuation due to treatment related reason at or prior to Week 24	xx (xx%)	Xx (xx%)
Censored [1]	Xx (xx%)	Xx (xx%)
Proportion of Subjects Without Protocol Defined Virologic Failure or not discontinued due to treatment related reasons at or prior to Week 48		
Estimate	xx.x%	xx.x%
95% CI	(xx.x%, xx.x%)	(x.x%, x.x%)
Difference in Proportions[2]		
Estimated Difference	x.x%	
95% CI [3]	(x.x%, x.x%)	

Note: [1] Subjects who have not met the PDVF criteria and are ongoing in the study, or who have discontinued for non-treatment related reasons are censored.

Note: [2] Difference: Proportion on GSK'254 xxmg + 2NRTI's - Proportion on DTG 50mg + 2NRTIs.

Note: [3] Based on Greenwood's formula.

Shell VIR_T1

Table 4.xx
Summary of INI Mutations at Baseline and Time of PDVF or prior to week X

Treatment: Trt. A

Codon	Mutation	Baseline (N=xx)	Time of PDVF (N=xx)
A1	A1A (wild type)	xx (xx%)	xx (xx%)
	Any mutation	xx (xx%)	xx (xx%)
	Any A1B	xx (xx%)	xx (xx%)
	Any A1C	xx (xx%)	xx (xx%)
	A1B	xx (xx%)	xx (xx%)
	A1C	xx (xx%)	xx (xx%)
H2	H2H (wild type)	xx (xx%)	xx (xx%)
	Any mutation	xx (xx%)	xx (xx%)
	Any H2B	xx (xx%)	xx (xx%)
	Any H2C	xx (xx%)	xx (xx%)
	H2B	xx (xx%)	xx (xx%)
	H2C	xx (xx%)	xx (xx%)
	H2C/B	xx (xx%)	xx (xx%)
	H2H/B	xx (xx%)	xx (xx%)
...			

Treatment:

...

Note: Baseline resistance testing was carried out on whole blood samples collected at Day 1 or subsequent visit using Monogram GenoSure Archive assay, which provides genotypic data only. On study resistance testing

used standard plasma based genotypic and phenotypic resistance testing assays. Testing on Confirmed Virologic Withdrawal subjects used the initial elevated viral load ("SVW") sample. Any codon at which there is only wild-type has been omitted from this table. "Any mutation" refers to Pre-specified IN Substitutions Associated with Development of Resistance to INSTI Class.
Note: Refer to decision table "Listing of All Genotypic and Phenotypic Data" that shows what data is in scope for analyses.

Programming Note: Ordered by frequency of the “Any mutation” values within codon. “Any mutation” included refers to the list of prespecified IN substitutions in RAP.

Shell VIR_T2

Protocol: 208379

Population: PDVF

Table 4.xx
Summary of Major Mutations of NRTI, NNRTI and PI Classes
by region at Baseline and Time of PDVF

Region: NRTI
Treatment: Trt. A

Codon	Mutation	Baseline (N=xx)	Time of PDVF (N=xx)
A1	A1A (wild type)	xx (xx%)	xx (xx%)
	Any mutation	xx (xx%)	xx (xx%)
	Any A1B	xx (xx%)	xx (xx%)
	Any A1C	xx (xx%)	xx (xx%)
	A1B	xx (xx%)	xx (xx%)
	A1C	xx (xx%)	xx (xx%)
H2	H2H (wild type)	xx (xx%)	xx (xx%)
	Any mutation	xx (xx%)	xx (xx%)
	Any H2B	xx (xx%)	xx (xx%)
	Any H2C	xx (xx%)	xx (xx%)
	H2B	xx (xx%)	xx (xx%)
	H2C	xx (xx%)	xx (xx%)
	H2C/B	xx (xx%)	xx (xx%)
	H2H/B	xx (xx%)	xx (xx%)
...			

Treatment: Trt. B
...

Class: NRTI

Class: NNRTI

Class: PI

Note: Baseline resistance testing was carried out on whole blood samples collected at Day 1 or subsequent visit using Monogram GenoSure Archive assay, which provides genotypic data only. On study resistance testing used standard plasma based genotypic and phenotypic resistance testing assays. Testing on Confirmed Virologic Withdrawal subjects typically uses the initial elevated viral load "SVW" sample. Any codon at which there is only wild-type has been omitted from this table.
Note: Major resistance mutations to classes NRTI, NNRTI, and PI are defined by the International Antiviral Society-USA (IAS-USA).
Note: Refer to decision table "Listing of All Genotypic and Phenotypic Data" that shows what data is in scope for analyses.

Programming Note: Repeat for other drug classes; ordered by frequency of the “Any mutation” values within codon.

Shell VIR_T4

Protocol: 208379

Population: PDVF

Table 4.xx

Summary of Phenotypic Susceptibility by Drug and Drug Class at the Time of PDVF for subjects meeting PDVF criteria

Class Drug Phenotype	Trt A (N=XX)	Trt B (N=XX)
INSTI		
DTG		
n	xx	xx
Sensitive	xx (xx%)	xx (xx%)
Resistant	xx (xx%)	xx (xx%)
BIC		
n	xx	xx
Sensitive	xx (xx%)	xx (xx%)
Resistant	xx (xx%)	xx (xx%)
EVG		
n	xx	xx
Sensitive	xx (xx%)	xx (xx%)
Resistant	xx (xx%)	xx (xx%)
RAL		
n	xx	xx
Sensitive	xx (xx%)	xx (xx%)
Resistant	xx (xx%)	xx (xx%)
NRTI		
DLV		
n	xx	xx
Sensitive	xx (xx%)	xx (xx%)
Resistant	xx (xx%)	xx (xx%)

Note: Time of PDVF is at the time of on-treatment initial suspected viral load sample, which was subsequently confirmed.

Shell VIR_T6

Protocol: 208379
Population: PDVF

Table 4.xx
Summary of Fold Change of IC50 at - Time of PDVF at or prior to Week 24

Drug		Trt A (N=xx)	Trt B (N=xx)
GSK254	Fold Change (class)		
	n	xxx	xxx
	0-<1	xx (xx%)	xx (xx%)
	2-<4	xx (xx%)	xx (xx%)
	4-<8	xx (xx%)	xx (xx%)
	>=8	xx (xx%)	xx (xx%)
	Fold Change		
	n	xxx	xxx
	Geom. Mean	x.xx	x.xx
	CV (%)	x.xxx	x.xxx
	Median	x.xx	x.xx
	Q1	x.xx	x.xx
	Q3	x.xx	x.xx
	Min.	x.xx	x.xx
	Max.	x.xx	x.xx
3TC	Fold Change (class)		
	n	xxx	xxx
	0-<1	xx (xx%)	xx (xx%)

...

Note: CV (Coefficient of Variation) = 100*sqrt(exp((SD on log scale)^2)-1).
Note: Time of PDVF is at the time of on-treatment initial suspected viral load sample, which was subsequently confirmed.
Note: Refer to decision table "Listing of All Genotypic and Phenotypic Data" that shows what data is in scope.

Shell VIR_L1

Protocol: 208379 Page 1 of n

Population:

Listing x
Listing of All Genotypic Data

Treatment: Trt A

Site ID/ Unique Subject ID	Date/ Nominal Visit/ Actual Analysis Visit	Time Point	Protease	Reverse Transcriptase	Integrase	PRO/RT Assay	IN Assay
PPD	PPD / SCREEN/ Screening	Screening	V3I, I15V, G17D, E35D, M36I, S37N, R41K, R57K, Q61D, L63H, A71T, I72R, I93L E297K,	K11R, V35T, T39L, I135V, D177E, I178V, G196E, L214F, V245L, V276I, R277K, A288S, K311R,		GenoSure	GenoSure
PPD	PPD /	On-treatment	V3I, K14N,	V35T, T39L,		VIROSEQ	

Treatment: Trt B
...

Note: * Major Mutation
Note: If available use PSGT and GSIN data for PRO/RT and IN regions first.
Note: If PSGT and GSIN data is not available for PRO/RT and IN regions use the available data from PSGT+IN.
Note: Refer to decision table "Listing of All Genotypic and Phenotypic Data" that shows what data is in scope.

Shell PRF1

Protocol: 208379

Population: EGD Sub Study

Summary of Gastric Biopsy Findings by Stomach Region and EGD Grading at Baseline and Week 24

Actual relative time	Stomach region Gastric Biopsy Findings	GSK254 XXmg + 2NRTIs (N=XX)	GSK254 XXmg + 2NRTIs (N=XX)	GSK254 XXmg + 2NRTIs (N=XX)	DTG XXmg + 2NRTIs (N=XX)	Total
Baseline/Week 24	Greater Curvature	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Normal	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Abnormal	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Single cell necrosis, parietal cells	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Chief cell atrophy or cytoplasmic alteration	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	…..					
	Dysplasia	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Lesser Curvature (Transitional Zone)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Normal	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Abnormal	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Single cell necrosis, parietal cells	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Chief cell atrophy or cytoplasmic alteration	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
…					
Dysplasia	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Note: Spasmolytic Polypeptid essing Meta ia (SPEM), E astroduodenosco D)
Note: EGD Grading: Grade 0 (CCI),Grade 1 (CCI), Grade 2 (CCI) and Grade 3 (CCI).
Note: EGD Findings Data base ndependent ologyst's Re
Progarmming Note: This table would incude all the stomach regions in Planned and Unplanned Biopsy

Shell PRF2

Protocol: 208379

Population: EGD Sub Study

Summary of Treatment Emergent Gastric Biopsy Findings by Stomach Region and EGD Grading at Week 24

Stomach region Gastric Biopsy Findings	GSK254 XXmg + 2NRTIs (N=XX)	GSK254 XXmg + 2NRTIs (N=XX)	GSK254 XXmg + 2NRTIs (N=XX)	DTG XXmg + 2NRTIs (N=XX)	Total
Greater Curvature	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Normal	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Abnormal	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Single cell necrosis, parietal cells	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Chief cell atrophy or cytoplasmic alteration	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
…..					
Dysplasia	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Lesser Curvature (Transitional Zone)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Normal	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Abnormal	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Single cell necrosis, parietal cells	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Chief cell atrophy or cytoplasmic alteration	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
…					
Dysplasia	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Grade 3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Note: Spasmolytic Polypeptide-Expressing Metaplasia (SPEM), Esophagogastroduodenoscopy (EGD)
Note: EGD Grading: Grade 0 (CCI),Grade 1 (CCI), Grade 2 (CCI and Grade 3 (CCI .
Note: Emergent refers to Gastric Biopsy Findings severity that develops or increases in intensity after baseline.
Note: EGD Findings Data based on Independent Pathologyst's Report
Progarmming Note: This table would incude all the stomach regions in Planned and Unplanned Biopsy
Progarmming Note: Ensure only Emergent cases are include in this table. if the same finding remains the same grade at baseline and week 24 then it will be excluded.

Shell PRF3

Protocol: 208379

Population: EGD Sub Study

Summary of Staining Methods by Visit

Actual Relative time	Staining Methods		GSK254 XXmg + 2NRTIs (N=XX)	GSK254 XXmg + 2NRTIs (N=XX)	GSK254 XXmg + 2NRTIs (N=XX)	DTG XXmg + 2NRTIs (N=XX)	Total
Baseline/ Week 24							
	Periodic Acid Schiff-Alcian Blue (PAS-AB)						
		Acceptable	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Not Acceptable	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Control Periodic Acid Schiff-Alcian Blue (PAS-AB)	Acceptable	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Not Acceptable	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Hematoxylin and eosin (H&E)	Acceptable	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Not Acceptable	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Reason why H&E Not acceptable						
		Any Reason	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Acceptable	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Crushing Artefact	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Inadequate Fixation	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Insufficient Tissue					

Note: EGD Data based on Independent Pathologyst's Report

Progarmming Note: This table would incude all the stomach regions in Planned and Unplanned Biopsy

Progarmming Note: Ensure only Emergent cases are include in this table. if the same finding remains the same grade at baseline and week 24 then it will be excluded.

Shell EGD1

Protocol: 208379

Population: EGD Sub Study

Summary of Esophagus and Stomach Vizualisation and Savary-Miller Grades

		GSK254 XXmg + 2NRTIs (N=XX)	GSK254 XXmg + 2NRTIs (N=XX)	GSK254 XXmg + 2NRTIs (N=XX)	DTG XXmg + 2NRTIs (N=XX)	Total
Savary-Miller Grades						
	Grade 1: Single Erosion Above The Gastroesophageal Mucosal Junction	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 2: Multiple Noncirumferential Erosions Above The Gastroesophageal Mucosal Junction	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 3: Circumferential Erosion Above The Mucosal Junction	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 4: Chronic Change With Esophageal Ulceration And Associated Stricture	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Grade 5: Barretts Esophagus With Histologically Confirmed Intestinal Differentiation Within The Columnar Epithelium	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Esophagus Vizualisation						
	Adequate	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Inadequate	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Reason for inadequate visualization of esophagus:					
	Reason #1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Reason #2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Reason #3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Stomach Vizualisation						
	Adequate	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Inadequate	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Reason for inadequate visualization of stomach:					
Reason #1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Reason #2	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Reason #3	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Note: Data based on Investigator's EGD eCRF data

Shell EGD2

Protocol: 208379
Population: EGD Sub Study

Summary of EGD Findings by Esophagus and Stomach Regions and Location of greatest impact by Grade at Baseline and Week 24

Treatment: GSK254 XXmg + 2NRTIs (N=XX)

Actual relative time	Region	EGD Findings Location of greatest impact:	Mild	Moderate	Severe	Total
Baseline/Week 24	Esophagus	Any Finding	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Nodules				
		Any location	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Upper Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Middle Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Lower Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		…				
		Early neoplastic finding				
		Any location	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Upper Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Middle Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Lower Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Stomach	Any Finding	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Erythema				
		Any location	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Gastric Cardia	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Fundus of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Lesser Curvature of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Greater Curvature of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
		Body of Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Pylorus of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
…				
Nodules				
Any location	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Gastric Cardia	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Fundus of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Lesser Curvature of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Greater Curvature of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Body of Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Pylorus of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Note: Data based on Investigator's EGD eCRF data

Progarmming Notes:
This table would incude any other findings reported for Stomach and Esophagus in the eCRF.

Repeat for all the 4 treatment arms.

Shell EGD3

Protocol: 208379

Population: EGD Sub Study

Summary of Treatment Emergent EGD Findings by Esophagus and Stomach Regions and Location of greatest impact by Grade at Week 24

Treatment: GSK254 XXmg + 2NRTIs (N=XX)

Region	EGD Findings Location of greatest impact:	Mild	Moderate	Severe	Total
Esophagus	Any Finding	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Nodules				
	Any location	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Upper Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Middle Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Lower Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	…				
	Early neoplastic finding				
	Any location	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Upper Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Middle Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Lower Third	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Stomach	Any Finding	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Erythema				
	Any location	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Gastric Cardia	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Fundus of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Lesser Curvature of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
	Greater Curvature of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Body of Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Pylorus of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
…				
Nodules				
Any location	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Gastric Cardia	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Fundus of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Lesser Curvature of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Greater Curvature of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Body of Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Pylorus of the Stomach	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Note: Data based on Investigator's EGD eCRF data

Progarmming Notes: This table would incude any other findings reported for Stomach and Esophagus in the eCRF. Repeat for all the 4 treatment arms.
Progarmming Note: Ensure only Emergent cases are include in this table. if the same finding remains the same grade at baseline and week 24 then it will be excluded.

Shell PRF4

Protocol: 208379

Population: EGD sub study

Listing X

Listing of Gastric Biopsy (PRF)

Site Id.: PPD

Treatment	Unique Subject Id./ Subject Id.	Age (YEARS)/ Sex/ Race Detail/ Weight (kg)	Stomach Region/ Gastric Biopsy Findings	Actual Relative time (Visit and date)	Emergent Flag	Grade	Staining Method/Decision
Trt A	PPD						

Shell EGD4

Protocol: 208379

Population:

Listing X

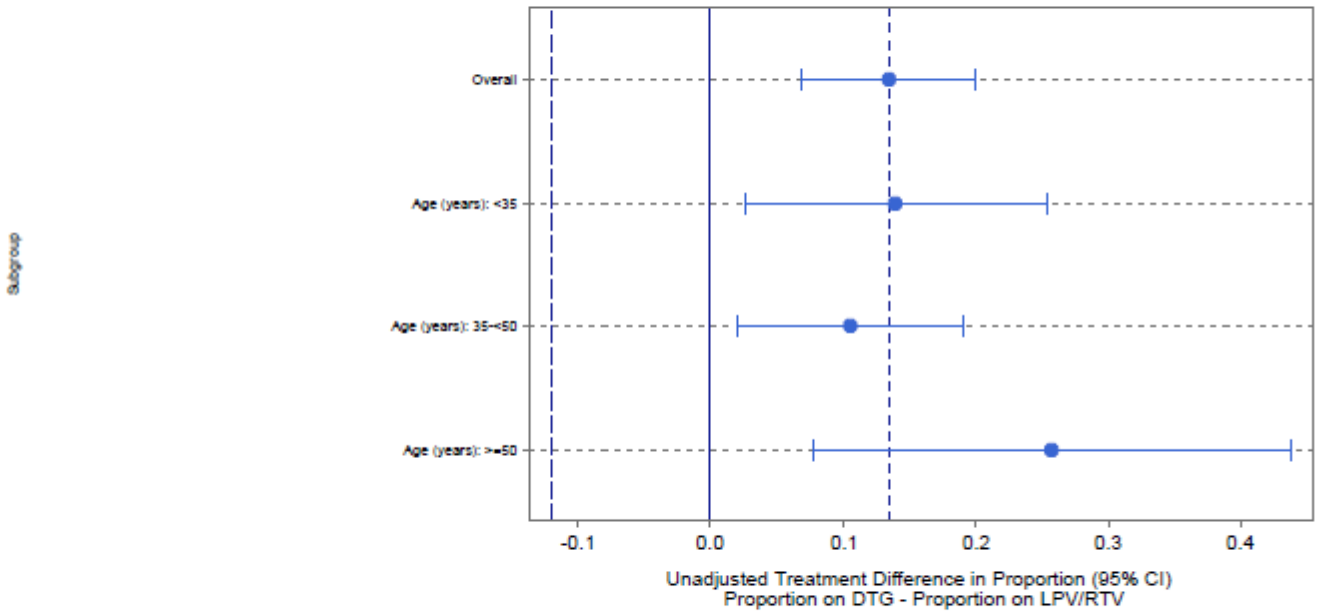
Listing of EGD Findings (CRF)

Treatment	Unique Subject Id./ Subject Id.	Age (YEARS)/ Sex/ Race Detail/ Weight (kg)	Region/EGD Findings/ Location of greatest impact	Actual Relative time	Emergent Flag	Grade	Savary-Miller Grades	Vizualisation / Reason if Inadequate
Trt A	PPD							

Shell 7

Protocol: 200304
Population: Intent-to-Treat Exposed

Figure 2.2
Unadjusted Treatment Difference in Proportion (95% CI) of Subjects with
Plasma HIV-1 RNA <50 c/mL at Week 48 by Subgroup - Snapshot Analysis



Note: The dashed reference line on the left at -0.12 represents the non-inferiority margin.
The dashed reference line on the right represents the overall difference in proportion (DTG - LPV/RTV).
PPD /arenv/arprod/gsk1349572/mid200304/primary_01/drivers/f_adsnap_202.sas 23MAR2018 19:51