Division: World Wide Development

Retention Category: GRS019

Information Type: Reporting and Analysis Plan

Title:	Reporting and Analysis Plan Amendment 5 for study 200056 A Phase IIb Study Evaluating a Long-Acting Intramuscular Regimen of GSK1265744 plus TMC278 for The Maintenance of Virologic Suppression Following an Induction of Virologic Suppression on an Oral regimen of GSK1265744 plus Abacavir/Lamivudine in HIV-1 Infected, Antiretroviral Therapy-Naive Adult Subjects

Compound Number: GSK1265744

Effective Date: 05-Mar-2018

Description: This reporting and analysis plan contains a description of all planned statistical analyses and data summary for study 200056. A Phase IIb, randomized, multicentre, parallel group, open-label, three-part study to be conducted in approximately 265 HIV-1 infected ART-naive adults. This study will consist of Screening Period, 20 week Induction Period utilizing an oral regimen of GSK744 30 mg once daily plus ABC/3TC 600/300 mg once daily, Maintenance Period, Extension Period and a Long-term Follow-up Period. Subjects who have demonstrated tolerability to the Induction Period regimen and with an undetectable HIV-1 RNA (<50 c/mL) at the Week (-4) visit are eligible to enter the Maintenance Period. At Day 1, the Maintenance Period begins. Eligible subjects will be randomized 2:2:1 to receive an IM regimen of GSK744 LA 400 mg + TMC278 LA 600 mg every 4 weeks for 96 weeks, an IM regimen of GSK744 LA 600 mg + TMC278 LA 900 mg every 8 weeks for 96 weeks, or to continue on the oral Induction Period regimen of GSK744 30 mg + ABC/3TC once daily for 96 weeks. Subjects who successfully complete 96 weeks of CAB LA + RPV LA treatment in the Maintenance Period will continue with their current IM dosing regimen of CAB LA and RPV LA in the Extension Period. Eligible subjects who successfully complete 96 weeks of CAB 30 mg + ABC/3TC treatment in the Maintenance Period will have the option to continue study participation by switching to an optimized IM dosing regimen of their choice (either Q8W or Q4W) of CAB LA + RPV LA in the Extension Period. Subject randomization will be stratified by subjects' HIV-1 RNA prior to Week (-8) (<50 c/mL, yes or no). **This fifth amendment includes amendments to the originally approved RAP and amendments 1, 2, 3 and 4.**

Subject: HIV-1 infection, GSK1265744, integrase inhibitor, abacavir, lamivudine, rilpivirine, TMC278, TMC278 LA, non-nucleoside reverse transcriptase inhibitor, therapy-naive, induction, maintenance, long-acting, LA, once daily, once monthly, every other month, Quality of Life, injectable, injection

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ABBREVIATIONS

3TC	Lamivudine, Epivir
ABC	Abacavir, Ziagen
AE	Adverse Event
AIC	Akaike Information Criteria
AIDS	Acquired immunodeficiency syndrome
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
ANOVA	Analysis of Variance
ART	Antiretroviral Therapy
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
AUC	Area Under the Curve
AUC(0 – τ)	Area under the plasma drug concentration-time curve from pre-dose to the end of the dosing interval at steady state
BUN	Blood urea nitrogen
C0	Pre-dose Concentration
Cτ	Concentration at the end of a dosing interval
c/mL	Copies/milliliter
CDC	Centers for disease control and prevention
CDM	Clinical Data Management
CI	Confidence Interval
CL/F	Apparent Oral Clearance
Cmax	Maximum plasma drug concentration
Cmin	Minimum plasma drug concentration
CMV	Cytomegalovirus
CNS	Central Nervous System
CPK	Creatine Phosphokinase
CPMS	Clinical Pharmacology Modeling and Simulation
CSR	Clinical Study Report
CVb	Coefficient of Variation for Geometric Mean
dL	Deciliter
DAIDS	Division of Acquired Immunodeficiency Syndrome
DNA	Deoxyribonucleic acid
DTG	Dolutegravir
eCRF	Electronic case report form
Emax	Maximal Effect
ECG	Electrocardiograph
eCSSRS	Electronic Columbia Suicidality Severity Rating Scale
EFV	Efavirenz
ELV	Elvitegravir
FC	Fold change
FDA	US Food and Drug Administration
FDC	Fixed dose combination
FTC	Emtricitabine, Emtriva

GFR	Glomerular Filtration Rate
GI	Gastrointestinal
GSK	GlaxoSmithKline
H0	Null Hypothesis
H1	Alternative Hypothesis
HBV	Hepatitis B Virus
HGB	Hemoglobin
HCV	Hepatitis C Virus
HDL	High Density Lipoprotein
HIV-1	Human Immunodeficiency Virus Type 1
HPD	Highest Posterior Density
HR	Heart Rate
HSR	Abacavir Hypersensitivity Reaction
IAS	International AIDS Society
IB	Investigator's Brochure
IDSL	Integrated Data Standards Library
INI	Integrase Inhibitor
INR	International Normalized Ratio
IP	Investigational Product
iSRC	Internal Safety Review Committee
ITT-E	Intent-to-Treat Exposed
ITT-ME	Intent-to-Treat Maintenance Exposed
IU	International Unit
kg	Kilogram
L	Liter
LDL	Low Density Lipoprotein
LLQ	Lower Limit of Quantification
LOCF	Last Observation Carried Forward
LVH	Left ventricular hypertrophy
MCV	Mean Corpuscle Volume
MCH	Mean Corpuscle Hemoglobin
MCHC	Mean Corpuscle Hemoglobin Concentration
MedDRA	Medical Dictionary for Regulatory Activities
MSDF	Missing, Switch, Discontinuation equals Failure
mg	Milligram
mL	Milliliter
NCEP	National Cholesterol Education Program
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NQ	Not Quantified
NRTI	Nucleoside reverse transcriptase inhibitor
OC	Observed case
PD	Pharmacodynamic
PI	Protease Inhibitor
PK	Pharmacokinetics
PO	Taken Orally
PP	Per Protocol

PP-M	Per Protocol Maintenance
PRO	Protease
PT	Prothrombin Time
PTT	Partial Thromboplastin Time
QTc	Corrected QT interval
RAL	Raltegravir, Isentress, MK-0518
RAP	Reporting analysis plan
RBC	Red Blood Count
REML	Restricted Maximum Likelihood
RNA	Ribonucleic acid
ROC	Receiver Operating Characteristic
RPV	Rilpivirine hydrochloride
RT	Reverse transcriptase
RUCAM	Roussel Uclaf Causality Assessment Method
SAE	Serious adverse event
SD	Standard Deviation
SIA	Suicidal Indication Alert
SOC	System organ class
t1/2	Estimated terminal phase half-life
τ	Dosing interval, time between consecutive doses
TDF	Tenofovir disoproxil fumarate, Viread
tlag	Time between dosing and detectable plasma concentrations
tmax	Time at which Cmax was observed
tmin	Time at which Cmin was observed
TSH	Thyroid Stimulating Hormone
TST	Therapeutic Area Standard
ULN	Upper limit of normal
US/USA	United States/United States of America
WBC	White Blood Count
WT	Wild type virus

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to provide details of planned analyses and data displays for reporting results of study 200056. These analyses may be included in regulatory submissions, study reports, and publications.

In the first amendment to the RAP originally effective 19-FEB-2015, the following changes were made: adding the pre-specified dose regimen selection criteria for the Week 32 primary analysis, adding updated data displays for injection site reaction adverse events, adding details for the efficacy assessment of the comparability between the IM regimens (see Section 8.3.3.2 of the protocol), removing the correlation analysis for snapshot response and the HIVMQ response of medication adherence, removing subscales for the HIVTSQ questionnaire; added supportive pk concentration data displays excluding non-evaluable concentrations, and other additional miscellaneous clarifications.

In the second amendment to RAP amendment #1 effective 18-SEP-2015, the following changes were made prior to the Week 48 interim analysis:

- Correction to the formula for the CKD-EPI GFR derivation (Section 9.2.7); previous formula had 'min and min' which has been corrected to 'min and max';
- Added further subdivision of the second Baseline HIV-1 RNA subgroup (Section 8.3); replacing '≥ 100,000' with '≥ 100,000 to <200,000; ≥ 200,000';
- Addition of a figure to summarize the proportion of subjects with virologic failure by visit based on the Snapshot (MSDF) algorithm (Section 11.3 and Section 17.2.2.2);
- Addition of an exploratory summary of the proportion of subjects with plasma HIV-1 RNA <2 copies/mL by visit (observed case dataset) according to the BioMontr low-level assay (Section 11.3.1 and Section 17.2.2.1, Section 17.2.2.4)
- Removed the following PK table from the Table of Contents for Data Displays (Section 17.2.5.1): Summary of Results of GSK1265744 PK Parameters Comparison between Induction and Maintenance Phase;
- Added additional tables to summarize PK concentrations using log-transformed statistics (Section 14.1.1 and Section 17.2.5).
- Removed 'Listing of Positive eCSSRS Findings' from Section 17.2.3.4 and added the following tables to Section 17.2.3.1: 'Listing of eCSSRS Suicidal Ideation and Behaviour Data For Subjects With at least One Positive Response for Suicidal Indication Alert', 'Listing of eCSSRS Suicidal Behaviour Details For Subjects With at least One Positive Response for Suicidal Indication Alert', 'Listing of eCSSRS Details of Most Severe Suicidal Ideation For Subjects With at least One Positive Response for Suicidal Indication Alert'

- Removed 'Listing of Possible Suicidality-Related Adverse Event Data: Event and Description' from Section 17.2.3.4 as this is already included in Section 17.2.3.1.

- Removed 'Summary of Maintenance Period Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product' from Section 17.2.3.1 as this duplicates information contained in the 'Summary of Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product' table.

The analyses detailed in this document are based on the protocol of study 200056 effective on 13 June 2014.

In the third amendment to RAP amendment #2 effective 27-JAN-2016, the following changes were made prior to the Week 96 interim analysis based on the protocol amendment #5 effective on 21-JUN-2016:

- Updated study design schematic, objectives, and IDMC monitoring plan to align with updates contained within protocol amendment #5 (mostly notably: Q8W/Q4W arms to continue into Extension, Oral arm subjects to switch form oral treatment to optimized IM regimen treatment for the Extension Period).

- Added Extension Switch Population to align with Protocol Amendment #5;

- Updates to period slotting and visit slotting to address transition into the Extension period;

- Updates to certain study population and safety data displays to align with recent updates to core IDSL data display standards;

- Addition of a limited number of new displays to include Extension period data (see Section 17.2 Table of Contents for Data Display Specifications – Week 32/48/96)

- Addition of 'observed case' efficacy summary of the proportion of subjects with plasma HIV-1 RNA level below 50 copies/mL by treatment group and visit;

- Addition of data listing of quantitative plasma HIV-1 RNA data for subjects with HIV-1 RNA $\geq$ 50 c/mL at any time during the Maintenance Period or Extension Period;

- Addition on statistical analysis of HIVTSQs updated total score and individual item scores;

- Addition of summary of HIVMQ results combining separate responses for CAB LA and RPV LA into a combined score;

- Addition of limited PK tables/listings of LTFU period data;

- Addition of fold-changes results for DTG and EVG in summary tables of phenotypic data;

- Addition of new treatment group descriptors for data displays including extension period data;

- Updated Section 6.1.8 and Section 6.1.9 to clarify that the Safety Population is used for safety analyses of induction period data and that the Safety Maintenance Population is used as the primary population for safety analyses (except for induction period data).

- Other miscellaneous (title updates and re-numbering of data displays) in Section 17.2 Table of Contents for Data Display Specifications – Week 32/48/96.

In this fourth amendment to RAP amendment #3 effective 09-DEC-2016, the following changes were made prior to the Week 128 Extension Switch analysis based on the protocol amendment #5 effective on 21-JUN-2016:

- Added displays for the W128 Extension Switch reporting effort, focusing on the Extension Switch Population during the Extension Period up to Week 128.

- Added the definition for "Protocol Defined Virologic Failure (PDVF) Genotypic and Phenotypic Extension Switch Population" in Section 6.1.14 for analysis of Extension Period On-treatment and treatment-emergent genotype and phenotype.

- Added in Table 7 the "Total – Optimized IM" group in Section 7.4

- Updated in Section 9 that starting from the Week 96 analysis, SAS Version 9.4 is used for data manipulations, tabulations, and calculations.

- Added in Section 9.2.2 the definition of baseline value for the Extension Switch Population during the Extension Period.

- Updated in Section 9.2.4 that a subject's exposure can be presented in "number of injections" to investigational product in addition to in "days"

- Updated in Section 9.2.17 the derivation of "Long-Term Follow Up (LTFU) Study Day" of an event.

- Updated example b in Section 9.3 that the subject is Q4W rather than "Q4W/Q8W".

- Updated the Extension Period Assignment rule in Table 15 in Section 9.3.

- Update the date rage for study period assignment for Q4W/Q8W randomized subjects not receiving Extension period IP injection in Table 16 in Section 9.3.

- Updated the rule for Extension Period Day 1 assessment window assignment, and removed the "Week 121" nominal visit in Table 23 in Section 9.4.1.

- Updated the rules for LTFU Assessment Window assignment in Table 25 in Section 9.4.1.

- Added Table 26 to define the Assessment Windows for summary of snapshot (MSDF) data at key analysis time points for the Extension Switch Population.

- Updated in Section 12.7.2.2 the definition of Extension Period emergent toxicities.

- Added sampling windows for evaluable Extension Period PK concentrations for the Extension Switch Population in Table 31 in Section 14.1.1.

- Updated that for the Week 128 analysis, PK parameters will not be produced, and that the steady state analysis will not be performed given the small sample size in the Extension Switch Population as well as evidence from the Maintenance Phase that achievement of steady state occurred more than 28 weeks on LA treatment.

- Updated that the subsequent analysis to the W128 analysis will be at Week 160 instead of Week 152.

In this fifth amendment to RAP amendment #4 effective 30-Aug-2017, the following changes and minor administrative corrections were made prior to the Week 160 analysis based on the protocol amendment #7 effective on 16-Nov-2017:

- Added displays for the W160 reporting effort to characterize the long-term safety and efficacy profile for the randomized Q8W/Q4W IM population during the Maintenance and Extension Period, as well as for the Extension Switch Population during the Extension Period.

- Updated in Section 6.1.7 that the PK population will include all subjects who receive IP and undergo PK sampling during the study, and provide available GSK1265744 and /or TMC278 plasma concentration data.

- Added the definition for “Protocol Defined Virologic Failure (PDVF) Genotypic and Phenotypic Maintenance Exposed Population” in Section 6.1.12 for analysis of Maintenance and Extension Period genotype and phenotype at the time of PDVF.

- Updated in Section 7.4 that for the W160 analysis, descriptor “IM – Total” will be used instead of “Subtotal – IM” unless otherwise noted.

- Updated in Table 26 the assessment windows for summary of snapshot (MSDF) data at W160 for the Extension Switch Population.

- Added in Table 27 the assessment windows for summary of snapshot (MSDF) data at W160 for the randomized IM subjects who continued Q8W/Q4W IM dosing during the Extension Period

- Updated in Section 9.1.1.2 that the observed case viral load for assessment is the value that is closest to the target date.

- Updated in Table 23 the assessment window assignment of the Extension Period data to the Follow Up Period for the Extension Switch Subjects

- Updated in Section 12.7.2.2 the definition of treatment emergence relative to induction baseline and relative to maintenance baseline.

This RAP is based on the standard operating procedure SOP_54838 (formerly SOP-WWD-4000) v03, effective 28 September 2007, regarding the Development, Review and Approval of Reporting and Analysis Plans. This RAP was written using the document standard INS_51933 (formerly INS-WWD-4000) v04, effective 26 June 2008. Any deviation(s) from this RAP will be described in the clinical study report (CSR).

2. STUDY OBJECTIVE(S) AND ENDPOINT(S)

Objective	Endpoint
Primary	
To select an intramuscular dosing regimen of GSK744 LA plus TMC278 LA based on a comparison of the Week 32 antiviral activity, tolerability, and safety of two IM dosing regimens, relative to GSK744 30 mg plus ABC/3TC orally once daily.	The proportion of subjects with HIV-1 RNA <50 c/mL at Maintenance Week 32 based on intent to treat-maintenance exposed (ITT-ME) population using the Missing, Switch, or Discontinuation = Failure (MSDF) algorithm. Proportion of subjects with protocol defined virologic failures over time
	Incidence and severity of AEs and laboratory abnormalities over time.
Secondary	
To evaluate the antiviral activity, tolerability, and safety of GSK744 30 mg plus ABC/3TC orally once daily through the Induction and Maintenance Periods.	Proportion of subjects with plasma HIV-1 RNA <200 c/mL and <50 c/mL over time. Absolute values and change from Baseline in plasma HIV-1 RNA. Absolute values and changes from Baseline in CD4+ cell counts. Incidence of disease progression (HIV-associated conditions, acquired immunodeficiency syndrome [AIDS] and death). Incidence and severity of AEs and laboratory abnormalities over time. Absolute values and changes in laboratory parameters over time.
To evaluate the efficacy, tolerability, and safety of GSK744 LA 400 mg IM plus TMC278 LA 600 mg IM every 4 weeks and GSK744 LA 600 mg IM plus TMC278 LA 900 mg every 8 weeks, relative to GSK744 30 mg plus ABC/3TC orally once daily, through Week 96 of the Maintenance Period.	Proportion of subjects with plasma HIV-1 RNA <200 c/mL and <50 c/mL over time. Proportion of subjects with protocol defined virologic failures over time.
	Absolute values and change from Baseline in plasma HIV-1 RNA.
	Absolute values and changes from Baseline in CD4+ cell counts.
	Incidence of disease progression (HIV-associated conditions, acquired immunodeficiency syndrome [AIDS] and death.

Objective	Endpoint
	Incidence and severity of AEs and laboratory abnormalities over time.
	Absolute values and changes in laboratory parameters over time.
To characterize GSK744 LA and TMC278 LA PK and to explore PK-PD relationships.	Plasma PK parameters for GSK744 LA and TMC278 LA (C_{trough}, concentrations post dose [~Cmax]) during the Maintenance Period. Plasma GSK744 and RPV trough concentrations will be used to determine when steady state is achieved for each GSK744 LA and TMC278 LA regimen. Relationship between plasma PK parameters and plasma HIV-1 RNA, CD4+ cell counts and/or occurrence of adverse events [AEs] through Week 48 of the Maintenance Period will be explored.
To assess the development of viral resistance in subjects experiencing protocol defined virologic failure.	Incidence of treatment emergent genotypic and phenotypic resistance to GSK1265744, TMC278, and other on-study ART.
To explore the effect of various demographic Baseline characteristics and adherence on virologic response of GSK1265744 and TMC278 over time.	Proportion of subjects with plasma HIV-1 RNA <50 c/mL over time.
To evaluate the treatment satisfaction for subjects on the long-acting injectable regimens with those on the oral regimen through Week 96 of the Maintenance Period.	Summarize treatment satisfaction using the HIV Treatment Satisfaction Questionnaire Status (HIVTSQ(s)) over time.
To evaluate the change in treatment satisfaction for subjects in both the long-acting injectable and oral regimens through Week 32 of the Maintenance Period.	Measure change in treatment satisfaction using the HIV Treatment Satisfaction Questionnaire Change (HIVTSQ(c)) over time.
To evaluate medication adherence over time.	Summarize subject reported medication adherence using the HIV Medication Questionnaire (HIVMQ) over time.
Exploratory	
To evaluate the efficacy, tolerability, and safety of optimized IM dosing regimens CAB LA 400 mg IM plus RPV LA 600 mg IM every 4 weeks and CAB LA 600 mg IM plus RPV LA 900 mg every 8 weeks at Weeks 128 and 160 for subjects switching from the oral regimen	Proportion of subjects with a 'virologic failure' endpoint as per FDA Snapshot algorithm at Week 128 and 160 (Missing, Switch or Discontinuation = Failure, Extension Switch population) Proportion of subjects with Plasma HIV-1 RNA

Objective	Endpoint
therapy at the end of the Maintenance Period. To evaluate the long term efficacy, tolerability, and safety of IM dosing regimens CAB LA 400 mg IM plus RPV LA 600 mg IM every 4 weeks and CAB LA 600 mg IM plus RPV LA 900 mg every 8 weeks at Week 160 for subjects who continued randomized IM dosing in the Extension Period.	<50 copies/mL (c/mL) at Week 128 and 160 using the FDA Snapshot algorithm (Extension Switch population) Proportion of subjects with protocol defined virologic failures over time Proportion of subjects with plasma HIV-1 RNA <200 c/mL and <50 c/mL over time. Absolute values and changes in CD4+ cell counts over time Incidence of disease progression (HIV-associated conditions, acquired immunodeficiency syndrome [AIDS] and death). Incidence and severity of AEs and laboratory abnormalities over time. Absolute values and changes in laboratory parameters over time.

2.1. Statistical Hypotheses

The study is designed to evaluate the efficacy and safety of GSK744 LA 400 mg IM plus TMC278 LA 600 mg IM every 4 weeks and GSK744 LA 600 mg IM plus TMC278 LA 900 mg IM every 8 weeks, relative to GSK744 30 mg once daily plus ABC/3TC once daily, through Week 32 of the Maintenance Period.

To claim positive outcome, the following hypotheses will be tested for each of the IM regimen:

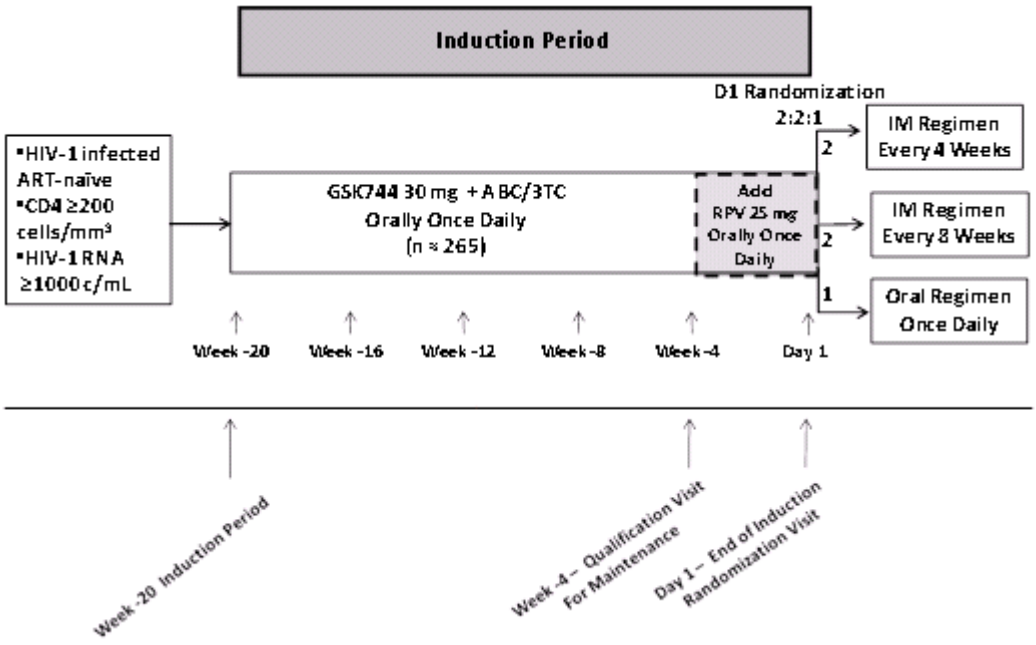
H_0: Response rate for GSK744 LA plus TMC278 LA two-drug regimen ≤ GSK744 plus ABC/3TC -10%

H_1: Response rate for GSK744 LA plus TMC278 LA two-drug regimen > GSK744 plus ABC/3TC -10%

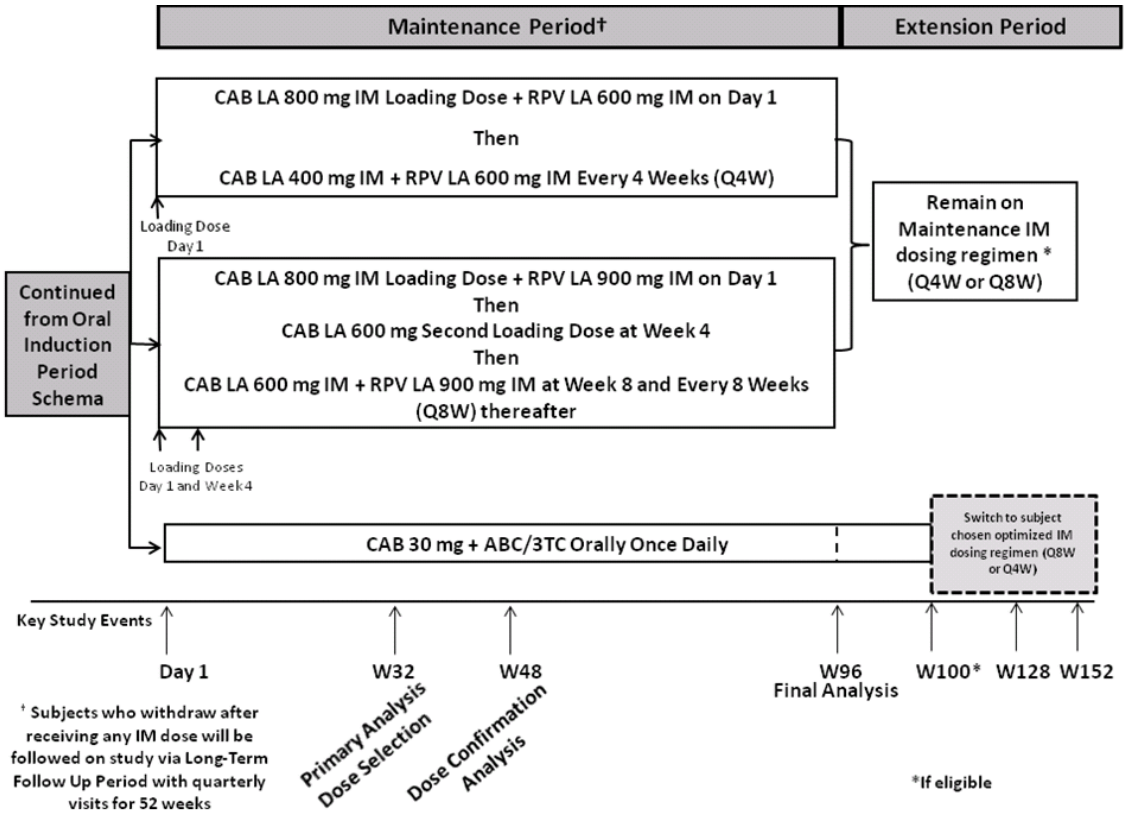
3. STUDY DESIGN

3.1. Study Design Schematic

Induction Period



Maintenance and Extension Period



3.2. Study Design

Study 200056 is a Phase IIb, randomized, multicentre, parallel group, open-label, three-part study in HIV-1 infected ART-naive adults. The study will enroll approximately 265 subjects in order to randomize approximately 225 subjects at Day 1.

This study will consist of a Screening Period, Induction Period, Maintenance Period, Extension Period and a Long-term Follow-up Period (withdrawn IM subjects only).

A subject is considered to have completed the study if they complete the Induction and Maintenance Period through Week 96.

3.2.1. Screening Period

Subjects will participate in a screening period of up to 28 days. Subjects may be re-screened once. Subjects who are randomized into the trial and subsequently withdrawn from the study, for any reason, may not be re-screened. Subjects may be randomized as soon as all eligibility requirements have been met. Subjects who are *HLA-B*5701* positive at the Screening visit are allowed to enter the study on a dual-NRTI backbone that does not contain abacavir.

3.2.2. Induction Period

Following the Screening Period, eligible subjects will be enrolled into the study and begin a 20 week Induction Period utilizing an oral regimen of GSK744 30 mg once daily plus ABC/3TC 600/300 mg once daily.

Week -20 is considered the Baseline visit and is the first day on study treatment. Further weeks of treatment throughout the Induction Period will be counted up to Day 1 (Day 1 initiates the Maintenance Period).

Example:

First day on study Week (-20)

Next visit Week (-16)

Next visit Week (-12), etc

Subjects will initiate treatment at Baseline (Week -20) and will be seen every 4 weeks for study treatment dispensing and safety and efficacy assessments. Unless subjects meet a study withdrawal criteria, their regimen will be modified at Week (-4) with the addition of RPV 25 mg once daily for the remainder of the Induction Period.

3.2.3. Maintenance Period

At Day 1, the Maintenance Period begins. Eligible subjects will be randomized 2:2:1 to receive an IM regimen of GSK744 LA 400 mg + TMC278 LA 600 mg every 4 weeks for 96 weeks, an IM regimen of GSK744 LA 600 mg + TMC278 LA 900 mg every 8 weeks for 96 weeks, or to continue on the oral Induction Period regimen of GSK744 30 mg + ABC/3TC once daily for 96 weeks (or 100 weeks if continuing on to the Extension Period). Subject randomization will be stratified by subjects' HIV-1 RNA prior to Week (-8) (<50 c/mL, yes or no).

3.2.4. Extension Period

Both IM randomized dosing regimens (Q8W and Q4W) will continue to be evaluated in the Extension period. Subjects who successfully complete 96 weeks of CAB 30 mg + ABC/3TC treatment in the Maintenance Period with an undetectable HIV-1 RNA (<50 c/mL) at the Week 96 visit will have the option of continuing study participation by switching to an optimized IM dosing regimen of their choice (either Q8W or Q4W).

Subjects who successfully complete 96 weeks of CAB LA + RPV LA treatment (Q8W or Q4W) in the Maintenance Period will remain on their current regimen after Week 96 and will continue to receive their Maintenance Period IM dosing regimen for the remainder of study participation. Safety and efficacy assessments will be conducted every 16 weeks. Dosing visits will occur according to the selected dosing regimen.

All subjects who successfully complete 96 weeks of CAB 30 mg + ABC/3TC treatment in the Maintenance Period will have the option to continue study participation by switching to the optimized IM dosing regimen of their choice (either Q8W or Q4W) of CAB LA + RPV LA in the Extension Period. Subjects not choosing to switch to an optimized long acting regimen will complete their study participation at Week 96. See protocol for eligibility criteria for the Extension Period for subjects entering from the CAB 30 mg + ABC/3TC arm and details regarding the optimized IM dosing regimens. Subjects not eligible to enter the Extension Period will end their study participation.

3.2.5. Long-term Follow-Up Period – IM Regimens only

Any subject who receives at least a single dose of GSK744 LA and/or TMC278 LA and discontinues the GSK744 LA + TMC278 LA regimen for any reason must remain on suppressive HAART for at least 52 weeks after the last dose of GSK744 LA and/or TMC278 LA in order to prevent selective pressure on HIV and the potential for selection of resistant mutants. This period is considered study participation and subjects will be followed on study during this time.

3.2.6. Follow Up Visit

A Follow up visit may be conducted approximately 4 weeks after the last dose of IP and is required only if the subject has ongoing AEs or lab abnormalities at the last on-study visit. This visit is not required for subjects in the Long-Term Follow Up Period.

4. PLANNED ANALYSES

4.1. Interim and Final Analysis

The ITT-ME population will be primary efficacy population and the safety population will be the primary safety population for all analyses. All available data will be included in all interim analyses, including data beyond the designated time point except for the Day 1 analysis, if preformed, will only include data from the Induction Period.

The first IDMC planned in the protocol was based on the estimated enrolment period of 6 months. Thus at the first interim analysis the IDMC should evaluate the efficacy, safety and tolerability of GSK1265744 to determine if the GSK1265744 regimen is suboptimal such that it should be discontinued before all subjects transition into the Maintenance Period of the study. Due to the rapid enrolment, study recruitment finished in 3 months, the first IDMC review will be after all subjects have transitioned to Maintenance Period of the study. Full details of the analyses, estimated timing and the decision criteria that will be used to determine regimen performance will be pre-specified in the IDMC Charter.

This interim analysis schedule does not require an adjustment for multiplicity since there is no possibility of a false positive finding at any of the interim analyses conducted before Week 32, and since the Week 48 and 96 analyses will be used to further characterise the long-term safety and efficacy profile of GSK1265744. As no hypothesis is being tested

for rejection during the constant monitoring of virologic response, no adjustment for multiplicity will be performed.

4.2. IDMC Interim Analyses

The purpose of these analyses is for the Independent Data Monitoring Committee (IDMC) to evaluate the efficacy, safety and tolerability of GSK1265744 at early time points in the study. Due to the rapid enrolment of study, the first IDMC review will be after all subjects have transitioned to Maintenance Period of the study. Full details of the analyses, estimated timing and the decision criteria that will be used to determine regimen performance will be pre-specified in the IDMC Charter, with IDMC agreement.

All of the IDMC reviews will be produced by a Statistics and Data Analysis Centre (SDAC).

4.3. Futility Interim Monitoring

Continuous monitoring of the number of protocol defined virologic failures during the Maintenance Period and a futility interim analysis when 50% subjects have completed Week 24 is planned.

Continuous monitoring of the number of protocol defined virologic failures for subjects switching from oral CAB 30 mg + ABC/3TC to the optimized IM dosing regimen of their choice (Q8W or Q4W) will also be monitored during the Extension Period.

Continuous Monitoring

Plasma HIV-1 RNA data will be monitored closely as subjects enter the Maintenance Period in order to prevent subjects from continuing on a regimen if existing data indicates that they are at unacceptable risk of inadequate maintenance of virologic suppression. The number of protocol defined virologic failures during the Maintenance Period will be monitored in all subjects that have at least 4 weeks of either of the Maintenance Period IM dosing regimens (Week 4). If the number of failures meets or exceeds the thresholds specified in the table below (Table 1), this will be considered strong evidence of an inadequate response and will trigger a comprehensive IDMC data review and possible discontinuation of that treatment arm. If an inadequate response is seen in any arm and it is determined by IDMC that that arm should be discontinued, then subjects on that treatment arm can be switched to the remaining IM arm.

Table 1 Number of protocol-defined virologic failures on Maintenance Period that constitute strong evidence of inadequate virologic response

Number of subjects that had at least four weeks of maintenance dose on IM	Number of protocol-defined virologic failures after maintenance dose on IM
3-21	>=3
22-32	>=4
33-43	>=5
44-54	>=6
55-65	>=7
66-75	>=8
76-86	>=9
87-97	>=10
98-100	>=11

The thresholds described in this table are derived on the basis of the ratio of the likelihoods for the null hypothesis (H_0) that there is a subgroup of subjects with inadequate maintenance of virologic suppression and the alternative hypothesis (H_1) that the only virologic failures in the study are due to poor compliance. For this analysis, H_0 translates to a protocol defined virologic failure rate of 20% or higher (as defined in protocol Section 4.6) and H_1 translates to an expected 3% rate of protocol defined virologic failures. For the first IDMC review, if the true rate of virologic failure is 20% as specified in H_0, the probability to detect the inadequate virologic suppression is greater than 70%. If the true rate of virologic failure is 3%, the probability to see number of virologic failures exceed the threshold is less than<1%. Further details on this method are contained in the IDMC charter. Each threshold represents strong evidence in favour of H_0 over H_1 [Royall, 1997].

The scenarios described above are not exhaustive – it is possible that the overall virologic failure rate does not meet the threshold but that a subgroup of subjects (e.g. with a given combination of mutations or fold resistance to GSK1265744 above an as yet unknown threshold) are consistently experiencing virologic failure. GSK will monitor virologic response by Baseline genotype and may halt one or more treatment arms if at any time subjects are deemed to be at an unacceptable risk of an inadequate response on the basis of such monitoring, although the high number of possible genotypic subgroups precludes pre-specification of precise thresholds for such action.

The number of protocol defined virologic failures will also be monitored in subjects switching from oral CAB 30 mg + ABC/3TC to the optimized IM dosing regimen of their choice (Optimized Q8W or Optimized Q4W) during the Extension Period. For subjects that have at least 4 weeks of treatment with an optimized IM dosing regimen, if the number of protocol defined virologic failures meets or exceeds the thresholds specified in the table below (Table 2) prior to all subjects completing Week160, this will be considered strong evidence of an inadequate response and will trigger a comprehensive IDMC data review. If an inadequate response is seen in any arm and it is determined by IDMC that that arm should be discontinued, then subjects on that treatment arm can be switched to the remaining IM dosing regimens.

Table 2 Number of protocol-defined virologic failures for each Extension Period optimized IM dosing regimen that constitutes strong evidence of inadequate virologic response – Subjects switching from Maintenance oral CAB + ABC/3TC only

Number of subjects with at least four weeks of IM dosing	Number of protocol-defined virologic failures needed to trigger IDMC review
3-21	>=3
22-32	>=4
33-43	>=5
44-54	>=6

Futility Analysis after 50% of subjects complete Week 24

An interim analysis for the purpose of review by the IDMC will be performed after approximately 50% of subjects complete Week 24. A futility rule based on a Bayesian posterior probability approach will be applied to assess the probability that an IM treatment arm demonstrates comparability with the oral control arm given the partial data set. Posterior probabilities of success (Prob ($p_{IM} > p_{oral} - 0.1 \mid$ data)) are provided in Table 3 for a subset of possible outcomes that could occur at the interim. Those outcomes associated with a posterior probability of success <40% may trigger a comprehensive IDMC data review and possible discontinuation of that treatment arm, although all data will be taken into consideration for making this decision.

Table 3 Posterior Probability of Successa at the Interim Analysis Under Various Scenarios

# Successes in IM arm (out of 45)									
		35 (78%)	36 (80%)	37 (82%)	38 (84%)	39 (87%)	40 (89%)	41 (91%)	42 (93%)
# Successes in Oral arm (out of 23)	18 (78%)	0.564	0.678	0.753	0.850	0.913	0.955	0.979	0.993
	19 (83%)	0.454	0.558	0.679	0.782	0.859	0.931	0.966	0.986
	20 (87%)	0.346	0.465	0.574	0.694	0.805	0.890	0.942	0.974
	21 (91%)	0.244	0.348	0.455	0.584	0.706	0.829	0.907	0.961
	22 (96%)	0.146	0.231	0.335	0.461	0.604	0.736	0.845	0.926
	23 (100%)	0.081	0.135	0.218	0.324	0.473	0.612	0.755	0.874

a. Posterior probability of success is defined as (prob($p_{IM} > p_{oral} - 0.1 \mid$ data)) with informative prior Beta (23,2) for oral arm and non-informative prior Beta (1,1) for IM arm.

b. Highlighted cells represent outcomes with posterior probability <0.4 that may trigger a comprehensive IDMC data review.

The proposed futility analysis has 91% chance to discontinue the IM treatment arm at the interim analysis if the true response rates are 92% and 72% for the oral arm and IM arm, respectively. The power to discontinuing the IM treatment arm is 46% if the true response rates are 92% and 82% for the oral arm and IM arm, respectively. The chance

of discontinue the IM treatment in error is 2% if the true response rates are 92% for both the oral arm and IM arm.

4.4. Day 1 Interim Analysis

A Day 1 interim analysis may be conducted to support regulatory submissions and/or scientific conference presentations once the last randomized subject has completed the Day 1 study visit and the database has been cleaned and released for analysis. The results of this analysis will be used to evaluate efficacy, safety and tolerability of GSK744 30 mg once daily plus ABC/3TC once daily in the Induction Period. Only data from the Induction Period would be summarized in this analysis. One data cut when all subjects have completed Day 1 visit will be used for both the first IDMC review and Day 1 interim analysis, data from the Maintenance Period will be included in the IDMC review but will not be summarized or listed for the Day 1 interim analysis.

4.5. Week 32 Primary Analysis

The Week 32 primary analysis will be conducted once the last randomized subject has completed the Week 32 study visit and the database has been cleaned and released for analysis. The results of this analysis will be used to characterize safety, tolerability and durability of antiviral response of both IM dosing regimens of GSK744 LA + TMC278 LA and to select a regimen for further development should both IM dosing regimens be comparable to the oral control arm.

4.6. Week 48 Interim Analysis

The Week 48 interim analysis will be conducted once the last randomized subject has completed the Week 48 study visit and the database has been cleaned and released for analysis. The results of this analysis will be used to characterize the safety, tolerability and durability of antiviral response of both IM dosing regimens of GSK744 LA + TMC278 LA and to confirm the selected regimen for further development should both IM dosing regimens be comparable to the oral control arm.

4.7. Week 96 Final Analysis

The Week 96 final analysis will be conducted once the last randomized subject has completed the Week 96 study visit and the database has been cleaned and released for analysis. The results of this analysis will be used to fully characterise the long term safety and efficacy profile of both IM dosing regimens of GSK744 LA and TMC278 LA.

Follow-up analyses after the Week 96 analysis of data collected after subjects have switched to the chosen dose of GSK744 LA may be conducted to more fully characterize the long-term safety and efficacy profile of GSK744 LA.

4.8. Week 128 Extension Switch Analysis

The Week 128 analysis will be conducted once the last randomized subject has completed the Week 128 study visit and the database has been cleaned and released for analysis. The results of this analysis will be used to characterize the efficacy, tolerability, and safety of optimized IM dosing regimens for subjects switching from the oral regimen therapy at the end of the Maintenance Period.

4.9. Week 160 Analysis

The Week 160 analysis will be conducted once the last randomized subject has completed the Week 160 study visit and the database has been cleaned and released for analysis. The results of this analysis will be used to characterize the following: (a) the long-term safety and efficacy profile of both IM dosing regimens for subjects who continued randomized IM dosing in the Extension Period and (b) the safety, tolerability and durability of antiviral response of the optimized IM dosing regimens for subjects switching from the oral regimen therapy at the end of the Maintenance Period.

Follow-up analyses after the Week 160 analysis may be conducted to more fully characterize the long-term safety and efficacy profile of CAB LA + RPV LA dosing regimens.

5. SAMPLE SIZE CONSIDERATIONS

5.1. Sample Size Assumptions

IM treatment relative to Oral treatment

The sample size of 45 subjects in the oral treatment arm and 90 subjects each in the IM treatment arms were chosen to ensure a high probability that a long-acting two drug treatment with truly poor response relative to GSK744 once daily plus ABC/3TC once daily will not be studied further, while allowing for formal considerations of other factors should efficacy be similar between the treatment arms. It is assumed that 85% of subjects enrolled will be suppressed at Week (-16), therefore, initially approximately 265 subjects will be enrolled in order to have 225 subjects randomized at Day 1.

The study is designed to test the comparability of GSK744 LA plus TMC278 LA two-drug regimen to oral GSK744 30 mg once daily plus ABC/3TC. The primary comparison of interest will be performed using a Bayesian probability model. If the posterior probability that the difference is greater than -10% is large (i.e., ≥90%), then sufficient statistical evidence has been provided for the positive outcome. A response rate of 82% in the GSK744 LA plus TMC278 LA two-drug regimen (compared with an GSK744 plus ABC/3TC response rate of 92%) would result in a rejection of the null hypothesis with a probability of approximately 0.064 (type I error). The given sample size is unlikely to select a random sample that would falsely conclude that GSK744 LA plus TMC278 LA two-drug regimen is comparable with GSK744 plus ABC/3TC if the response rates are truly 82% versus 92%, respectively. If the GSK744 LA plus TMC278

LA two-drug regimen yields a response rate of greater than 92%, then there is a high probability of rejecting the null hypothesis and correctly concluding that GSK744 LA plus TMC278 LA two-drug regimen is at least as good as GSK744 plus ABC/3TC.

Historical response rates of dolutegravir, an integrase compound similar to GSK744, were used as reference for the oral control arm. Response rates for dolutegravir plus ABC/3TC ranged from 92% to 94% at Week 60 in studies SPRING-1, SPRING-2 and SINGLE among subjects who were suppressed (HIV-1 viral load <50 c/mL) at Week 24.

The probability of a positive outcome assuming the true response rate for GSK744 LA plus TMC278 LA two-drug regimen is presented in Table 4.

Table 4 Probability of Positive Outcome Assuming True Response Rates of GSK744 LA plus TMC278 LA

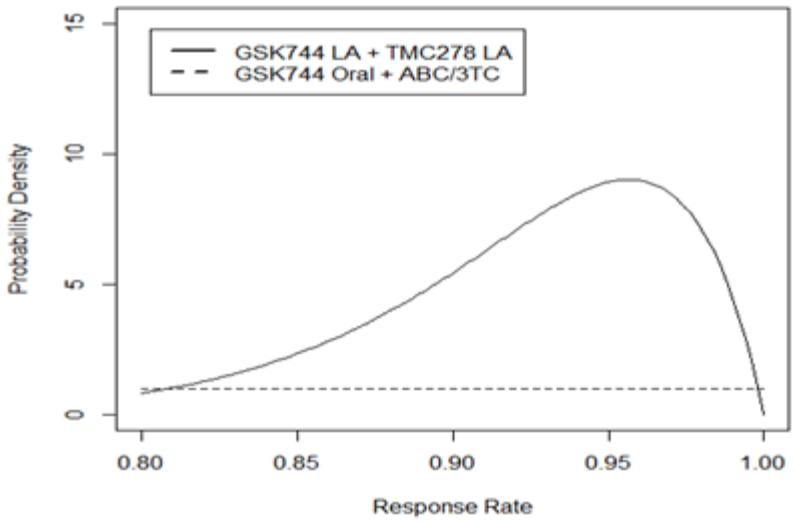
True Response Rate for GSK744 LA plus TMC278 LA two-drug regimen (Q4W or Q8W)	80%	82%[a]	86%	90%	92%	94%	96%
Probability of Positive Outcome[b]	2.8%	6.4%	26%	63%	82%	95%	99%

a. Type I error is <10%.
b. It is assumed that the response rate for GSK744 plus ABC/3TC is 92%.

Incorporation of prior beliefs and information about population parameters is a required part of any Bayesian probability model. The assumptions made will help provide a more reliable estimate when the prior beliefs are combined with the observed data than the data alone as long as the beliefs are reasonable. Therefore, the trial will utilize a Beta (23, 2) distribution with the mean response rate being 92%, with 97.5th percentile of 99% and 2.5th percentile of 78%.

Furthermore, a non- informative prior belief is assumed for the response rate for GSK744 LA plus TMC278 LA two-drug regimen. Therefore, the trial will conservatively utilize a Beta (1, 1) distribution. These priors are displayed in Figure 1.

Figure 1 **Plot of Prior Distribution for Response Rate for GSK744 LA plus TMC278 LA two-drug regimen and GSK744 plus ABC/3TC**

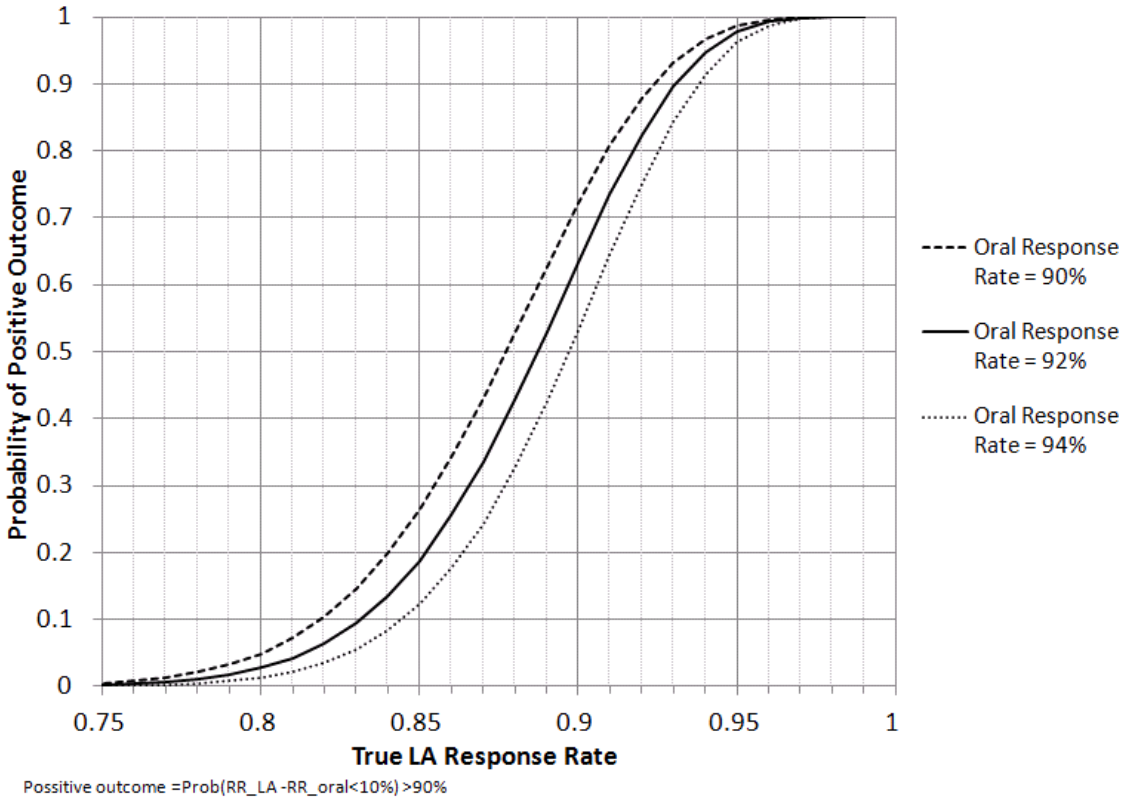


5.2. Sample Size Sensitivity

Long Acting IM treatment relative to Oral treatment

The operating characteristic (power) curve is used to evaluate any decision criteria (Bayesian and non-Bayesian alike). The operating characteristic curve for the proposed sample sizes for each treatment arm and prior information is shown in Figure 2.

Figure 2 Operating Characteristic Curve of Probability of Positive Outcome of GSK744 LA plus TMC278 LA two-drug regimen and GSK744 plus ABC/3TC



5.3. Sample Size Re-estimation

No sample size re-estimation is planned for this study.

6. ANALYSIS POPULATIONS

6.1. Analysis Populations

6.1.1. All Subjects Screened Population

The All Subjects Screened population will consist of all subjects screened for inclusion in the study.

6.1.2. Randomized Population

The Randomized population will consist of all subjects who are randomized in the study and will be used for select Study Population data listings.

6.1.3. Intent-to-Treat Exposed Population (ITT-E)

The ITT-E population consists of all enrolled subjects who receive at least one dose of IP. Subjects will be analyzed according to their randomized treatment regardless of what treatment was actually received. Those that are not randomized (i.e., withdrawn from the Induction Period or not eligible for randomization into the Maintenance Period) will be summarized together under a 'Not Randomized' category. The ITT-E population will be the secondary population for some efficacy analyses.

6.1.4. Intent-to-Treat Maintenance Exposed Population (ITT-ME)

The ITT-ME population consists of all randomized subjects who receive at least one injection or one dose of IP during the Maintenance Period of the study (on or after Day 1 visit). Subjects who discontinue during the Induction Period or are not eligible to be randomized into the Maintenance Period will not be included in the ITT-ME population. Subjects will be analyzed according to the randomized treatment regardless of what treatment was actually received. Unless stated otherwise, the ITT-ME population will be the primary population for efficacy analyses.

6.1.5. Per Protocol Maintenance Exposed Population (PP-ME)

This population will consist of subjects in the ITT-ME population with the exception of those with protocol deviations as described in Section 10.2.3 before a specified analysis timepoint. For example, a subject with such a protocol deviation between Week 32 and Week 48 would not be excluded due to this deviation from the Week 32 PP-ME Population, but would be excluded from the Week 48 PP-ME Population.

6.1.6. The PP-ME Population may be used for a supporting analysis of the primary endpoint. Such a supporting analysis will not be performed if the PP-ME Population comprises more than 95% of the ITT-ME Population. Per Protocol Extension Switch Population (PP-ES)

This population will consist of subjects in the Extension Switch population with protocol deviations as described in Section 10.2.3 on or after the first administration of IM loading dose (Week 100).

The PP-ES Population may be used for a supporting analysis of the Week 128 interim and the Week 160 endpoints. Such a supporting analysis will not be performed if the PP-ES Population comprises more than 95% of the Extension Switch Population.

6.1.7. PK Population

The PK Population will include all subjects who receive GSK1265744 and / or TMC278 and undergo PK sampling during the study, and provide available GSK1265744 and /or TMC278 plasma concentration data. Subjects in this population will be included in the PK analysis.

6.1.8. Safety Population

The Safety Population consists of all enrolled subjects who received at least one dose of IP. Subjects will be analyzed according to the actual treatments received. Subjects will not be excluded from this population as a result of changes to the background regimen. All safety analyses of induction period data will be produced using the safety population.

6.1.9. Safety Maintenance Population

The Safety Maintenance Population consists of all subjects who entered the Maintenance period and received at least one dose of IP. Subjects will be analyzed according to the actual treatments received. The safety maintenance population will be the primary population for safety analysis (with the exception of induction period data).

6.1.10. Safety Long-Term Follow-up Population

The Safety Long-Term Follow-up Population consists of all subjects receiving at least one dose of GSK744 LA and/or TMC278 LA who have discontinued IP/withdrawn from maintenance period and have a least one Long-Term Follow-up period clinic visit. Subjects will be analyzed according to the actual treatments received during the maintenance period. This population will be used to produce additional safety displays of long-term follow-up period data.

6.1.11. Protocol Defined Virologic Failure (PDVF) Genotypic and Phenotypic Populations

The PDVF Genotypic and Phenotypic populations will consist of all subjects in the ITT-E population with available On-treatment genotypic and phenotypic resistance data, respectively, at time of protocol defined virologic failure. These populations will be used for analysis of On-treatment and treatment-emergent genotype and phenotype.

6.1.12. Protocol Defined Virologic Failure (PDVF) Genotypic and Phenotypic Maintenance Exposed Populations

The PDVF Genotypic and Phenotypic Maintenance Exposed populations will consist of all subjects in the ITT-ME population with available genotypic and phenotypic resistance data, respectively, at the time of protocol defined virologic failure. These populations will be used for the W160 analysis.

6.1.13. Extension Switch Population

The Extension Switch population will include all subjects randomized to the oral 30 mg + ABC/3TC arm who switch to and receive at least one dose of the optimized IM dosing regimen of their choice (either Q8W or Q4W) in the Extension Period.

The Extension Switch population will be used to evaluate safety and efficacy of the optimized IM dosing regimens during the Extension Period.

6.1.14. Protocol Defined Virologic Failure (PDVF) Genotypic and Phenotypic Extension Switch Population

The PDVF Genotypic and Phenotypic Extension Switch population will consist of all subjects in the Extension Switch population with available on-treatment genotypic and phenotypic resistance data, respectively, at time of protocol defined virologic failure during the Extension Period. This population will be used for analysis of Extension Period on-treatment and treatment-emergent genotype and phenotype.

6.2. Analysis Data Sets

6.2.1. Missing, Switch or Discontinuation = Failure (Snapshot)

Subjects' responses (e.g., <50 c/mL) will be calculated according to the FDA's snapshot algorithm. This algorithm treats all subjects without HIV-1 RNA data at the visit of interest (due to missing data or discontinuation of IP prior to visit window) as non – responders, as well as subjects who switch their concomitant ART prior to the visit of interest as follows:

- Background ART substitutions not permitted per protocol;
- Background ART substitutions permitted per protocol but prescribed while not suppressed (e.g., HIV-1 RNA ≥ 50 copies/mL based on last viral load at time of decision to switch), unless the decision to switch is documented as being on or before the first on-treatment visit where HIV-1 RNA is assessed.

Otherwise, virologic success or failure will be determined by the last available HIV-1 RNA assessment while the subject is on-treatment within the visit of interest window (Section 9.4).

See Section 9.2.10 for full details of this MSDF algorithm.

6.2.2. Observed Case

The observed case (OC) dataset uses only the data that is available at a particular timepoint, with no imputation for missing values. This data will be used for safety analyses, sensitivity analyses and analysis of health outcome endpoints, and certain efficacy summaries (e.g. HIV-associated conditions, HIV-1 RNA and CD4 over time).

7. TREATMENT COMPARISONS

7.1. Primary Comparisons of Interest

The primary efficacy analysis will be performed at Week 32 based on the proportion of subjects in the ITT-ME population with plasma HIV-1 RNA <50 c/mL using MSDF algorithm. The primary comparison of interest will be the response rate of each IM dosing arm to the oral control arm performed using a Bayesian probability model. The

probability of (Response rate for IM arm ≤Response rate for Oral arm -10%) will be calculated.

7.2. Other Comparisons of Interest

The analysis described in Section 7.1 will also be performed using the PP-ME population if the PP-M Population comprises less than 95% of the ITT-ME Population. The results will be compared for consistency with the results from the ITT-ME population.

The probability that the Q8W treatment arm is comparable to Q4W treatment arm will be provided using the Bayesian probability model for the proportion of subjects with plasma HIV-1 RNA level below 50 c/mL at Week 32 based on the MSDF algorithm. The posterior probability of comparability between two IM treatment arms will be produced, as follows:

Let:

X_{Q8W} = number of responders in the Q8W IM arm, and

X_{Q4W} = number of responders in the Q4W IM arm.

The binomial distribution is the assumed likelihood of the response data, as follows:

$$X_{Q8W} \sim \text{Binomial}\ (N_{Q8W}, P_{Q8W})$$

$$X_{Q4W} \sim \text{Binomial}\ (N_{Q4W}, P_{Q4W})$$

where X_{Q8W} and X_{Q4W} are the number of responders out of N_{Q8W} or N_{Q4W} subjects randomized to the Q8W IM or Q4W IM arms in the ITT-ME population, respectively, and P_{Q8W} and P_{Q4W} are parameters for the response probabilities for each arm.

For this analysis, the posterior probability of comparability in response rates for each IM arm is:

$$P_2 = P\ (|P_{Q8W} - P_{Q4W}| < 0.1 \mid \text{data})$$

where the following non-informative prior conjugate beta densities for the true response rates:

$$P_{Q8W} \sim \text{Beta}\ (1, 1)$$

$$P_{Q4W} \sim \text{Beta}\ (1, 1).$$

A posterior probability of at least 90% (i.e., P_2 >0.90) corresponds to “substantial evidence of positive outcome” and is chosen as the weight of evidence threshold for concluding that the two IM dosing regimens are equivalent.

The probability to meet this equivalence criterion as a function of the true response rates and N=110 per arm (updated approximate sample size based on actual enrolment in the

maintenance period) is presented in Table 5. If the true response rates for Q8W and Q4W regimens are both equal to 92%, then the probability of correctly concluding that the two IM regimens are equivalent is approximately 0.85. A response rate of 82% in the Q8W regimen compared with response rate of 92% for the Q4W regimen (or vice versa) would result in an erroneous conclusion of equivalence with a probability of approximately 0.10 (type I error).

Table 5 Probability of Concluding Equivalence between Q4W and Q8W IM Arms (N=110 per arm)

	True Response Rate for Q4W				
True Response Rate for Q8W	**88%**	**90%**	**92%**	**94%**	**96%**
78%	0.092[a]	0.043	0.017	0.0049	0.0011
80%	0.18	0.096[a]	0.044	0.016	0.0042
82%	0.30	0.19	0.10[a]	0.044	0.014
84%	0.45	0.33	0.21	0.11[a]	0.044
86%	0.59	0.51	0.37	0.23	0.11[a]
88%	**0.68**	0.67	0.57	0.42	0.25
90%	0.68	**0.77**	0.75	0.64	0.47
92%	0.58	0.76	**0.85**	0.84	0.72
94%	0.42	0.65	0.84	**0.93**	0.91
96%	0.25	0.47	0.72	0.91	**0.98**

a. Type I error

7.3. Regimen Selection Criteria

The Week 32 primary analysis will be used to select an IM dosing regimen for further development. Regimen selection will be based primarily on antiviral activity in conjunction with safety, tolerability, treatment satisfaction, virologic resistance and PK measures. Data from the Week 48 analysis will be used to confirm regimen selection.

The criteria that follow are guidelines selected to rule out a regimen in the absence of unexpectedly strong evidence in its favour from other endpoints. Regimen selection will take all efficacy, safety, health outcomes and pharmacokinetic data into consideration. However, the number of endpoints collected in this study and therefore being considered for regimen-selection preclude the pre-specification of go/no go thresholds for every endpoint. Consequently, these criteria are being pre-specified for a limited number of key endpoints: the primary efficacy comparison assessing comparability to the oral control arm, and four key measures for assessing the safety profile of the IM dosing regimens. Efficacy and Safety criteria will be assessed using the ITT-ME and Safety-ME populations, respectively.

7.3.1. Efficacy Criteria

An IM dosing regimen failing to demonstrate comparability to the oral arm in the primary efficacy analysis (See Section 8.3.3.1 of the protocol) will not be considered for further study unless safety or tolerability concerns rule out the other IM regimen or there is compelling evidence that the failures were not related to CAB exposure. Additionally, an IM regimen will not be ruled out based on efficacy if the primary comparison of interest

is deemed underpowered due to a lower than expected observed response rate for the oral control arm.

If both IM regimens are shown to be comparable to the oral control arm in the primary comparison (or indeterminate for reasons mentioned above), then the Q8W regimen will be selected for further evaluation.

7.3.2. Safety Criteria

- The proportion of subjects with **Grade 3 or 4 injection site reaction related adverse events (AEs)** occurring on-treatment during the Maintenance Period. An IM dosing regimen on which ≥ **14% more subjects (approximately 15 or more subjects)** experience such events relative to the other IM regimen will not be considered for further study.

- The proportion of subjects **Grade 3 or 4 non-injection site reaction related AEs occurring** on-treatment during the Maintenance Period. An IM dosing regimen on which **≥ 9% more subjects (approximately 10 or more subjects)** experience such events relative to the other IM dosing regimen will not be considered for further study, unless there is compelling evidence that the differences observed were not related to CAB exposure (e.g. based on evaluation of exposure/toxicity relationships, see Section 14.3.3).

- The proportion of subjects with **any serious adverse events (SAE)** occurring on-treatment during the Maintenance Period. An IM dosing regimen on which **≥ 9% more subjects (approximately 10 or more subjects)** experience any serious adverse event relative to the other IM dosing regimen will not be considered for further study, unless there is compelling evidence that the SAEs observed were not related to CAB exposure.

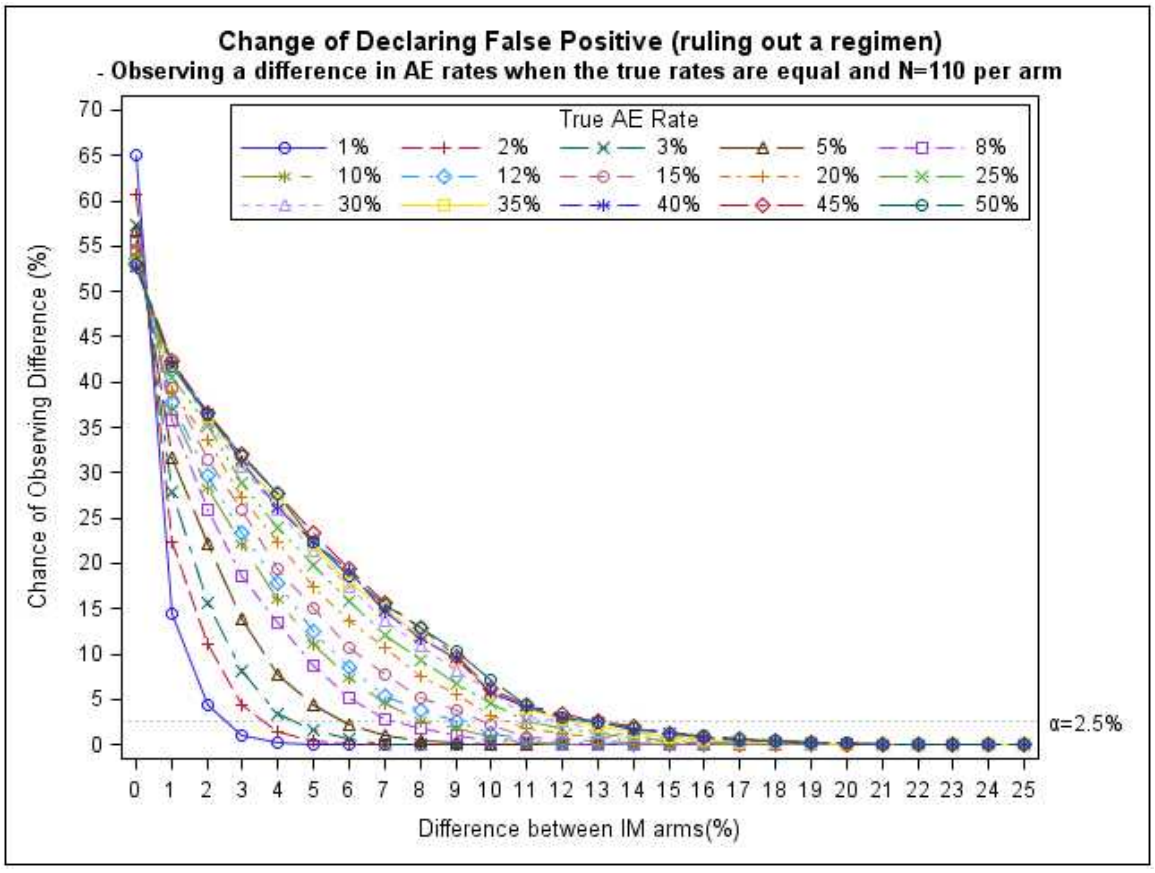
- The proportion of subjects with **treatment emergent Grade 3-4 ALT toxicities** during the Maintenance Period. An IM dosing regimen on which **≥4% more subjects (approximately 4 or more subjects)** experience such toxicities relative to the other IM dosing regimen will not be considered for further study, unless there is compelling evidence that the elevations observed were not related to CAB exposure (i.e. acute hepatitis, evidence for significant alcohol consumption, dehydration, illicit drug use, etc, and) .

- The proportion of subjects with any treatment emergent **Grade 3-4 laboratory toxicities** during the Maintenance Period. An IM dosing regimen on which **≥8% more subjects (approximately 9 or more subjects)** experience such toxicities relative to the other IM dosing regimen will not be considered for further study, unless there is compelling evidence that the differences observed were not related to CAB exposure (i.e. acute hepatitis, evidence for significant alcohol consumption, dehydration, illicit drug use, etc).

During the data review, smaller differences between the groups could still result in selecting the other IM dosing regimen, depending on the type of events observed.

NOTE: The % differences in the safety criteria are chosen so that the chance of seeing a safety difference that warrants stopping a dose is less than 1 in 40 (<2.5%) assuming both GSK744 LA + TMC278 LA dosing regimens have the same ISR safety profile, i.e. chance of false positive is controlled at <2.5%. The figure below (Figure 3) shows the chance of declaring false positive with different true AE rates. For example, if the true AE rate is equal in both arms and is 3% (green curve), then an observed difference of 5% or more (i.e. 5 or more subjects out of 110 subjects) would keep the false positive error rate below 2.5% (dotted horizontal line); or if the true AE rate in both arms is 10% (red curve), then an observed difference of 9% or more (i.e. 10 or more subjects out of 110 subjects) will keep the false positive error rate<2.5%. In addition, for all the efficacy and safety criteria above, a clinical review will also be undertaken comparing the GSK744 LA + TMC278 LA data against the oral control arm data and against historical control data. The GSK1265744 team will assess the totality of the data in order to make the final dose selection decision.

Figure 3 Chance of Declaration of False Positive



7.4. Data Display Treatment and Other Sub-group Descriptors

In data summary displays, treatment groups will be defined as shown in Table 6.

Table 6 Data Display Treatment Descriptors

Treatment Group	Descriptor for non PK	Descriptor for Maintenance Phase PK
GSK744 30 mg + ABC/3TC once daily	Oral 744	Oral 744
GSK744 LA 600 mg + TMC278 LA 900 mg IM every 8 Weeks (Q8W)	Q8W IM	Q8W (744 600 mg + TMC278 900 mg) IM
GSK744 LA 400 mg + TMC278 LA 600 mg IM every 4 Weeks (Q4W)	Q4W IM	Q4W (744 400 mg + TMC278 600 mg) IM
Combined IM group	Subtotal - IM	NA
Not Randomized	Not Randomized	NA

In data summary displays of Extension Period, data for subjects switching from maintenance oral randomized treatment to either of the optimized IM regimens (i.e. according to the Extension Switch Population), treatment groups will be defined as shown in Table 7. For the W160 analysis, descriptor "IM – Total" will be used instead of "Subtotal – IM" unless otherwise noted.

Table 7 Data Display Treatment Descriptors for Extension Switch Population

Treatment Group	Descriptor
Optimized GSK744 LA 600 mg + TMC278 LA 900 mg IM every 8 Weeks (Q8W)	Optimized Q8W IM
Optimized GSK744 LA 400 mg + TMC278 LA 600 mg IM every 4 Weeks (Q4W)	Optimized Q4W IM
Combined Optimized IM group	Total – Optimized IM

In data listing displays, study treatment will be denoted by the expanded treatment arm descriptors shown in Table 8.

Table 8 Data Listings Display Treatment Descriptors

Treatment Arm	Descriptor for Data Listings
GSK744 LA 600 mg + TMC278 LA 900 mg IM every 8 Weeks (Q8W)	Q8W IM
GSK744 LA 400 mg + TMC278 LA 600 mg IM every 4 Weeks (Q4W)	Q4W IM
GSK744 30 mg + ABC/3TC once daily for Maintenance Period, selected GSK744 LA 600 mg + TMC278 LA 900 mg IM every 8 Weeks (Q8W) for Extension Period	Oral CAB Maintenance/Q8W Extension
GSK744 30 mg + ABC/3TC once daily for Maintenance Period, selected GSK744 LA 400 mg + TMC278 LA 600 mg IM every 4 Weeks (Q4W) for Extension Period	Oral CAB Maintenance/Q4W Extension

Treatment Arm	Descriptor for Data Listings
GSK744 30 mg + ABC/3TC once daily for Maintenance Period and did not participate in Extension Period	Oral CAB Maintenance/No Extension
Induction Period participation only, not randomized into Maintenance Period	Induction Period Only

In the event that subjects switch to another IM regimen from a regimen which is discontinued, an amendment to this RAP will be created to detail how such subjects will be described in data displays of subsequent analyses.

8. GENERAL CONSIDERATIONS FOR DATA ANALYSES

8.1. Multicentre Studies

The randomization for this study was not stratified or blocked by center. A centralized randomization schedule was employed. Data will be summarized for all centres combined.

8.2. Other Strata and Covariates

The randomization is stratified by subjects' HIV-1 RNA prior to Week (-8) (<50 c/mL, yes or no). A single change in background dual NRTI is permitted as described in the protocol, which, if necessary, is likely to occur early during therapy. Therefore the initial background dual NRTI may not accurately represent the predominant therapy received up to the time of analysis. Therefore, the subgroup analyses will be based on the background dual NRTI at Week -16 or time of IP discontinuation, whichever is earlier.

8.3. Examination of Subgroups

Summaries of antiviral response will be repeated by subgroups from the following list:

- Plasma HIV-1 RNA result prior to Week (-8) (<50 c/mL yes or no); related to investigator specified stratification factor but re-derived using laboratory values.
- Baseline plasma HIV-1 RNA:

  <100,000 or ≥100,000 c/mL;

  <1000; 1000 to <10,000; 10,000 to <50,000; 50,000 to <100,000; ≥100,000 c/mL to <200,000; ≥ 200,000;
- First suppressed (HIV-1 RNA <50 c/mL) at Week (-16), (-12), (-8), and (-4).

Summaries of antiviral response will be repeated by subgroups from the following list only if greater than 20% of the subjects overall fall into more than one subgroup level

- Background dual NRTI (ABC/3TC, TDF/FTC, Other) at Week -16 or time of IP discontinuation, whichever is earlier;

- Baseline CD4+ cell count: <200; 200 to <350; ≥ 350 cells/mm^3;
- Baseline Centers for Disease Control and Prevention (CDC) category (CDC Category A, CDC Category B, or CDC Category C);
- Race (white or non-white);
- Gender (female or male);
- Age (<50 or ≥50);
- Age (<65, ≥65 years)
- Known HIV risk factors or mode of transmission (injectable drug user, homosexual contact and not injectable drug user, or no homosexual contact and not injectable drug user).

8.4. Multiple Comparisons and Multiplicity

This interim analysis schedule does not require an adjustment for multiplicity since there is no possibility of a false positive finding at any of the interim analyses conducted before Week 32, and since the Week 48 and 96 analyses will be used to further characterise the long-term safety and efficacy profile of GSK1265744. As no hypothesis is being tested for rejection during the constant monitoring of virologic response, no adjustment for multiplicity will be performed.

8.5. Virology

Full sequence reverse transcriptase (RT), protease (PRO), and integrase (INI) data will be analyzed at baseline and at time of suspected protocol-defined virologic failure (PDVF) for baseline mutations and for treatment emergent mutations. These analyses will use the PDVF Genotypic population.

Phenotypic changes for approved drugs will be determined at baseline and at time of suspected PDVF. Treatment emergent phenotypic changes will be investigated in the PDVF Phenotypic population.

8.6. Genotype

An assessment will be made of every change across all amino acids within the INI encoding region at baseline and at time of suspected protocol-defined virologic failure, with particular attention paid to specific amino acid changes associated with the development of resistance to raltegravir (RAL), elvitegravir (ELV), dolutegravir (DTG) or GSK1265744. The known single and multiple INI mutations associated with the development of resistance to RAL, ELV, DTG or GSK1265744 are shown in Table 9.

Table 9 INI Mutations Associated with Development of Resistance to RAL, ELV, DTG or GSK1265744

Amino Acids in HIV Integrase for Analysis	H51Y, **T66A**, **T66I, T66K**, L68V, L68I, L74I, L74M, L74R, **E92Q, E92V**, Q95K, T97A, G118R, E138A, E138K, E138T, G140A, G140C, G140S, **Y143C, Y143H, Y143R,** P145S, S147G, **Q148H, Q148K, Q148R,** V151I, V151L, S153F, S153Y, **N155H,** E157Q, G163R, G163K, G193E, R263K

a. Note: draft listing; may be modified in case of additional substantive data availability.
b. IN substitutions listed **in bold** above were defined from http://hivdb6.stanford.edu with a score of >45. All other mutations were detected during INI clinical investigation or during in vitro studies with DTG.
c. The mutations bolded are referred to 'primary' mutations, and those unbolded are referred to 'secondary' mutations for this reporting and analysis.

Major resistance mutations to other classes (i.e., NRTI, NNRTI, PI) as defined by IAS-USA and shown in Table 10 will be evaluated at baseline and at time of suspected PDVF.

Table 10 Major Mutations Associated with Resistance to Other Classes

NRTIs	M41L, A62V, K65R/E/N, D67N, 69 insert, K70R/E, L74V, V75I, F77L, Y115F, F116Y, Q151M, M184V/I, L210W, T215Y/F, K219Q/E
NNRTIs	L100I, K101E/P, K103N/S, V106A/M, V108I, E138A/G/K/Q/R, V179L, Y181C/I/V, Y188C/L/H, G190S/A, H221Y, P225H, F227C, M230I/L
PIs	D30N, V32I, M46I/L, I47A/V, G48V, I50V/L, I54M/L, Q58E, T74P, L76V, V82A/T/F/L/S, N83D, I84V, N88S, L90M

Note: the most recent information available from IAS-USA guide [Wensing et al. 2017]will be used.

8.7. Phenotype

Phenotypic susceptibility to all licensed antiretroviral drugs and GSK1265744 will be determined using PhenoSense HIV assays from Monogram Inc. and will be reported as fold change (FC) in IC_{50} relative to wild-type control virus NL4-3, i.e., FC of sample virus = IC_{50} of sample virus/IC_{50} of control virus.

Since the maximum assay limit for FC for each ART varies from subject to subject, FC values that are greater than the maximum assay limit (e.g., '>100') will be interpreted as having a value equal to the smallest maximum assay limit for that ART in the study population for data analysis. Censored values will be presented 'as is' in the listings. Phenotypic susceptibilities will be categorised according to FC as shown in Table 11 (based on Monogram PhenoSense assay). Clinical cutoffs (where available) or biological cutoffs by PhenoSense will be used to define the phenotypic susceptibility of background treatment.

Replication capacity is generated as part of standard phenotypic assays.

Table 11 Clinical and Biological Cutoff Values for the PhenoSense HIV Drug Resistance Assay

Drug	Abbreviation	Class	PhenoSense cutoff
Abacavir	ABC	NRTI	(4.5 – 6.5)[a]
Lamivudine	3TC	NRTI	3.5[a]
Didanosine	ddI	NRTI	(1.3 – 2.2)[a]
Stavudine	d4T	NRTI	1.7[a]
Zidovudine	AZT (ZDV)	NRTI	1.9
Emtricitabine	FTC	NRTI	3.5
Tenofovir	TDF	NRTI	(1.4 – 4)[a]
Delavirdine	DLV	NNRTI	6.2
Efavirenz	EFV	NNRTI	3
Nevirapine	NVP	NNRTI	4.5
Etravirine	ETR	NNRTI	2.9[a]
Rilpivirine	RPV	NNRTI	2
Fosamprenavir/r	FPV/r	PI	4[a]
Atazanavir/r	ATV/r	PI	5.2[a]
Indinavir/r	IDV/r	PI	10[a]
Lopinavir/r	LPV/r	PI	(9 – 55)[a]
Nelfinavir	NFV	PI	3.6
Saquinavir/r	SQV/r	PI	(2.3 – 12)[a]
Tipranavir/r	TPV/r	PI	(2 – 8)[a]
Darunavir/r	DRV/r	PI	(10 – 90)[a]
Ritonavir	RTV	PI	2.5
Enfuvirtide	T20	FI	6.48
Raltegravir	RAL	INI	1.5
Elvitegravir	ELV	INI	2.5[b]
Dolutegravir	DTG	INI	(4 – 13)[a]
GSK1265744	744	INI	2.5[b]

a. clinical cutoff (lower cutoff – higher cutoff)
b. standard cutoff used by Monogram Inc. until clinical or biological cutoff has been determined

9. DATA HANDLING CONVENTIONS

All data manipulations, tabulations, and calculations will be performed using SAS Version 9.3, and SAS Version 9.4 starting from the Week 96 analysis on a system of Linux computers. Figures may also be produced using SAS or other clinical graphics software on the same system.

9.1. Premature Withdrawal and Missing Data

The method for dealing with premature withdrawals and missing data will depend on the endpoint being analysed. In the following sections methods are outlined and analysis strategies described.

9.1.1. Methods for Proportion Endpoints Based on Plasma HIV-1 RNA

9.1.1.1. Missing, Switch or Discontinuation = Failure (MSDF)

For each scheduled assessment time, the MSDF (also known as snapshot) response rate for a given threshold (e.g., <50 c/mL) is defined as:

$$\text{MSDF Rate} = \frac{\text{Number of responders in that analysis window}}{\text{Number of subjects in the analysis population}}$$

In each analysis window, a subject is defined as a responder as per the algorithm described in Section 9.2.10. In particular, if no HIV-1 RNA assessment is available for a subject in the assessment window, then that subject will be counted as a non-responder. The nature of this missing data will be further classified in MSDF summaries as either 'Virologic Failure' or 'No Virologic Data at Week X'; see Section 9.2.10 for full details.

9.1.1.2. Observed Case (OC)

For each scheduled assessment time, the OC rate for a given threshold is defined as:

$$\text{OC} = \frac{\begin{array}{c}\text{Number of subjects with a positive response (e.g. the closest - to - target viral load value}\\ \text{in the window below the threshold) at the timepoint, where the subject is still on treatment}\end{array}}{\begin{array}{c}\text{Number of subjects in the analysis population with an assessment in the scheduled}\\ \text{visit window during the treatment period}\end{array}}$$

9.1.1.3. Time to Event Methods

The time to virologic or tolerability failure [protocol defined virologic failure (PDVF) or discontinuation due to treatment related reasons (i.e., drug-related AE, protocol defined safety stopping criteria, or lack of efficacy)] will be calculated. Subjects who have not met PDVF criteria and are ongoing in the study, or who have discontinued for reasons other than those related to treatment, will be censored. Censored observations will be addressed in the analysis based on Kaplan-Maier survival analysis methods (See Section 11.2.5).

9.1.2. Methods for Health Outcomes Data

No imputations will be made for Health outcomes endpoints.

9.1.3. Method for Other Laboratory Data

For other laboratory data (HIV-1 RNA as a continuous measure, CD4+ and CD8+ cell counts, hematology, and clinical chemistry) no imputation for missing data or premature discontinuation will be performed and the observed values will be used. If more than one assessment was collected during the scheduled visit window, then the closest on-

treatment assessment to the scheduled visit will be summarized in the summary tables. If two assessments are equidistance and closest to the scheduled visit, then the later of the two assessments collected will be summarized in the summary tables.

9.1.4. Methods for Vital Signs and ECG Data

For other assessments such as vital signs and ECGs no imputation for missing data or premature discontinuation will be performed and the observed values will be used.

9.1.5. Methods for Missing PK Data

No imputations will be made for missing PK data.

9.1.6. Methods for Missing Dates

9.1.6.1. Date of Birth

Due to local privacy regulations, the electronic case report form (eCRF) only collect year of birth. All birth dates will be imputed as 30-Jun for month & day.

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.

In listings of demographic data, year of birth as entered will be displayed.

9.1.6.2. Adverse Events

The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event:

- For a missing start day, the 1st of the month will be used unless this is before the start date of investigational product; in this case the IP start date will be used (and hence the event is considered On-treatment, induction or maintenance, as per Section 9.3.1).
- For a missing stop day, the last day of the month (28th, 29th, 30th, or 31st as appropriate for the month and year) will be used, unless this is after the stop date of IP; in this case the IP stop date will be used.

Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.

In listings of AE data, the partial start and end dates as entered will be displayed.

9.1.6.3. Concomitant Medications

Missing dates for concomitant medications/ARTs are handled as described in Section 9.4.4

9.1.6.4. IP Exposure

A partial date, day of the month may be missing, is allowed for IP exposure stop date. The following method will be used to impute the missing day:

- For a missing stop day, the last day of the month (28th, 29th, 30th, or 31st as appropriate for the month and year) will be used, unless this is after the next start date of IP; in this case the next IP start date will be used.

9.1.6.5. HIV Condition

Partial dates are also allowed for the start date of the subject's HIV condition. No imputation will be performed on these partial dates.

9.2. Derived and Transformed Data

9.2.1. Age

Age, in whole years, will be calculated with respect to the date of the subject's Screening visit. For subjects with partial date of birth recorded in the eCRF, the imputed date of birth (Section 9.1.6) will be used to calculate the subject's age. If the date of birth is partial and the calculated age of the subject is 17, then the age will be changed to 18 if the site has indicated the subject had met the age eligibility requirement for the study (≥18 years of age).

9.2.2. Baseline and Change from Baseline

Unless stated otherwise, the baseline value for a parameter (including labs, vital signs, ECGs, virology assessments, etc.) for the study is defined as the last Pre-treatment (see Section 9.3) value observed. This is generally expected to be from the Week -20 visit, although such values may be missing or unscheduled assessments may be performed before treatment start.

Electrocardiograms (ECGs) are to be performed in triplicate on Week -20 visit. The baseline value for an ECG parameter will be the mean of the last pre-treatment set of assessments from the same date.

The baseline value for each period of the study is defined as the last value observed prior to the first treatment in each study period. E.g. for baseline for the Maintenance period is defined as the last value observed prior to the first injection for IM arms or oral dose at Day 1 for Oral arm.

Except for ECGs, the baseline value for the Extension Switch Population during the Extension Period is defined as the last value observed up to and including the date of the first IM exposure (loading dose) of CAB (if time of assessment is also collected, then time of assessment must be prior to time of injection). For ECGs, the baseline value for the Extension Switch Population during the Extension Period is defined as the last value prior to the date of the first IM exposure (loading dose) of CAB (since W100 ECGs were collected at any time during the visit per protocol, which may be before or after the first injection on that day). For the Extension Switch Population, any ECG values collected on or after the date of the first IM exposure (loading dose) will be considered as Extension period data when summarizing values during the Extension Period (e.g. ECG values collected on the date of first IM exposure of CAB will be slotted to analysis visit Week 100).

Change from baseline for a parameter is calculated as (observed value - baseline value).

The percentage change from baseline for a parameter is calculated as:

$$\%\,\text{change from baseline} = \frac{\text{observed value} - \text{baseline value}}{\text{baseline value}} \times 100$$

9.2.3. Corrected QT Intervals

When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fridericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements.

If RR interval (in msec) is provided then missing QTcB and/or QTcF will be derived as

$$\text{QTcB} = \frac{\text{QT}}{\sqrt{\text{RR}/1000}} \qquad \text{QTcF} = \frac{\text{QT}}{\sqrt[3]{\text{RR}/1000}}$$

where uncorrected QT interval is also measured in msec.

If RR interval is not provided directly and one of QTcB or QTcF has been entered, then RR interval can be obtained from the above formulas and used to calculate the other correction method value; i.e.,

$$\text{QTcB} = \sqrt{\frac{\text{QTcF}^3}{\text{QT}}} \qquad \text{QTcF} = \sqrt[3]{\text{QT} \cdot \text{QTcB}^2}$$

9.2.4. Exposure

A subject's exposure, in days or number of injections, to investigational product will be calculated as in the table below:

Study Period	Exposure
Induction	Exposure= 744 IP Stop Date – 744 IP Start Date + 1
Maintenance	Oral arm: Exposure= 744 IP Stop Date – 744 IP Start Date + 1
	IM arms: 744 Exposure = Number of 744 LA Injections received during the Maintenance Period TMC278 Exposure = Number of TMC278 LA Injections received during the Maintenance Period
Extension	744 Exposure = Number of 744 LA Injections received during the Extension Period TMC278 Exposure = Number of TMC278 LA Injections received during the Extension Period

where 744 IP Stop Date is the date of final oral dose of 744 IP received in the study period and 744 IP Start Date is the date of initial dose of 744 IP in the study. If 744 IP Stop Date is missing then, for purposes of calculating exposure, it will be imputed using the date of last visit or the recorded date of withdrawal/completion, whichever is earlier.

9.2.5. Framingham Risk Equation

The predicted probability, p, for time (t = 4,…,12 years) of coronary heart disease according to the Framingham equation [Anderson, 1991] is

$$p = 1 - \exp\left(-e^{u}\right)$$

where $u = \dfrac{\log(t) - \mu}{\sigma}$, with $\mu = 4.4181 + m$ and $\sigma = \exp(-0.3155 - 0.2784 \times m)$. The quantity m is calculated as

$$m = \begin{cases} a - 1.4792 \times \log(age) - 0.1759 \times I_d & \text{if male} \\ a - 5.8549 + 1.8515 \times \left[\log(age/74)\right]^2 - 0.3758 \times I_d & \text{if female} \end{cases}$$

where

$$a = 11.1122 - 0.9119 \times \log(SBP) - 0.2767 \times I_s \\ - 0.7181 \times \log(TC/HDL) - 0.5865 \times I_{LVH}$$

and

$$I_d = \begin{cases} 1 & \text{if diabetic subject} \\ 0 & \text{otherwise} \end{cases}$$

$$I_s = \begin{cases} 1 & \text{current or former smoker} \\ 0 & \text{otherwise} \end{cases}$$

SBP = systolic blood pressure (mmHg)

TC = total serum cholesterol

HDL = serum HDL cholesterol

$$I_{LVH} = \begin{cases} 1 & \text{definite ECG for left ventricular hypertrophy} \\ 0 & \text{otherwise} \end{cases}$$

with total cholesterol and HDL cholesterol measured in the same units.

A subject is classified as diabetic if current or past is indicated in the medical conditions eCRF for Type 1 or Type 2 diabetes mellitus or subject has taken anti-diabetic medication at any time during the study. The medical monitor will review the listing of unique concomitant medication terms before database freeze and select the anti-diabetic medications.

Smoking status is collected in the eCRF on Baseline. A current smoker is defined as currently smoking/using tobacco or has smoked/used tobacco within the previous 6 months; a former smoker is defined as previously smoked/used tobacco products and has not smoked/used tobacco products within the previous 6 months.

Definite ECG for left ventricular hypertrophy (LVH) is assessed based on current or past indication in the medical conditions eCRF for LVH.

This calculation will not be performed for subjects who have indicated current or past myocardial infarction conditions on the eCRF. These subjects will not be included in summary statistics of risk, but will be counted in the highest category of risk in the summary by category.

9.2.6. Genotype

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. Table 12 shows how different amino acid changes will be represented.

Table 12 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'

9.2.6.1. Treatment-Emergent Mutations

Treatment-emergent genotypic mutations are defined as mutations that appear between baseline and an On-treatment assessment (e.g., at time of protocol defined virologic failure).

9.2.7. Glomerular Filtration Rate (GFR)

The CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) method will be used to provide an estimate of GFR, in mL/min, as follows:

$$\begin{aligned}\text{GFR} &= 141 \times \min(\text{CRT}_{\text{mg/dL}}/\text{k},1)^{a} \times \max(\text{CRT}_{\text{mg/dL}}/\text{k},1)^{-1.209} \times 0.993^{\text{Age}} \times \\ &\quad [1.018 \text{ if Female}] \times [1.159 \text{ if Black}] \\ &= 141 \times \min(\text{CRT}_{\mu\text{mol/L}}/(88.4 \times \text{k}),1)^{a} \times \max(\text{CRT}_{\mu\text{mol/L}}/(88.4 \times \text{k}),1)^{-1.209} \times 0.993^{\text{Age}} \times \\ &\quad [1.018 \text{ if Female}] \times [1.159 \text{ if Black}]\end{aligned}$$

where age (in years) are at time of assessment, k is 0.7 for females and 0.9 for males, a is -0.329 for females and -0.411 for males, and $\text{CRT}_{\mu\text{mol/L}}$ is serum creatinine concentration in GSK standard units of μmol/L. $\text{CRT}_{\text{mg/dL}}$ is serum creatinine concentration in mg/dL, and $\text{CRT}_{\mu\text{mol/L}}$=88.4x $\text{CRT}_{\text{mg/dL}}$.

9.2.8. Hepatitis Status

Hepatitis C status will be determined using antibody (IgM or IgG) and/or hepatitis C virus (HCV) RNA assessments performed during screening or during the conduct of the study. If both antibody and virus RNA assessments are available, then the latter will take precedence and positive/negative status will be based on whether HCV RNA is detectable (i.e., ≥43 IU/mL [≥1.63 log IU/mL]) or not.

A subject will be considered positive for hepatitis B virus (HBV) if they have a positive surface antigen or detectable HBV DNA result during screening or during the conduct of the study.

Baseline hepatitis status will be based on laboratory assessments collected during the Screening Period (see Section 9.3).

9.2.9. Lab Toxicities

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 summarizing toxicity grades for such parameters, they will be categorised as in Table 13 according to whether they are above or below the midpoint of normal range.

Table 13 Categorization of Select Lab Parameters Relative to Midpoint of Normal Range

Parameter	Below Midpoint	Above Midpoint
Calcium	Hypocalcemia	Hypercalcemia
Fasted glucose	Hypoglycaemia	Hyperglycaemia
Sodium	Hyponatremia	Hypernatremia
Potassium	Hypokalemia	Hyperkalemia

9.2.10. Missing, Switch or Discontinuation = Failure (Snapshot) Algorithm

The FDA's "snapshot" algorithm is intended to be primarily a virologic assessment of the endpoint, and as such follows a "virology first" hierarchy.

Virologic Success (e.g., <50 c/mL) or Virologic Failure within an analysis window (see Section 9.4.1) is typically determined by the last available 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 a Virologic Success. Depending on the reason for lack of data, the subject will be classified as a Virologic Failure 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 Virologic Failure.

A subject may also be considered a Virologic Failure if they make changes to their background regimen. This includes:

- background ART substitutions not permitted per protocol;
- Background ART substitutions permitted per protocol but prescribed while not suppressed (e.g., HIV-1 RNA ≥ 50 copies/mL based on last viral load at time of decision to switch), unless the decision to switch is documented as being on or before the first on-treatment visit where HIV-1 RNA is assessed.

The addition of oral RPV in the induction period at week -4 is not considered switch nor substitution of background ART. Full details of the algorithm, including the handling of special cases, are included in Section 17.5.

9.2.11. PK Parameters

For the purposes of calculating summary statistics and for statistical analyses, all PK parameters with the exception of t_{max} will be $\log_e$ transformed.

Between-subject coefficient of variation (%CVb) will be calculated as follows:

$$\%CVb = 100 \times \sqrt{\exp[(\log_e \text{ transformed SD})^2] - 1}$$

9.2.12. 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. In cases where a sample has been retested, the retest 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.

9.2.13. CD4

CD4+ values provided as non-numeric, censored results from the central laboratory (e.g., '<0.02' in original units of GI/L) will be imputed as e.g. 0.019 so that they are converted to standard units of cells/mm^3 and included in the CD4 summary statistics. The listing will report the censored result as '<20' in the standard units, i.e., equivalent to <0.02 GI/L.

9.2.14. Post-baseline

Post-baseline refers to the combined time periods of On-treatment and Post-treatment (Section 9.3.1). Post-baseline may be further specified according to phase of the study: Randomized or Extension (Section 9.3.1).

9.2.15. Induction Period Study Day

The Induction Period Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the initial start date of IP in the Induction period as follows:

if date of event ≥ start date of Induction Period 744 IP, then

- Induction Period Study Day = date of event - start date of Induction period IP + 1

if date of event < start date of Induction Period 744IP, then

- Induction Period Study Day = date of event - start date of Induction period IP

Note that the initial start date of Induction period 744 IP is considered to be on Induction Period Study Day 1 and the day before this is Induction Period Study Day -1; i.e., there is no Induction Period Study Day 0.

9.2.16. Study Day

The Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the initial start date of 744 IP on Maintenance period as follows:

if date of event ≥ start date of IP, then

- Study Day = date of event - start date of 744 IP on Maintenanc e period + 1

if date of event < start date of IP, then

- Study Day = date of event - start date of 744 IP on Maintenanc e period

Note that the initial start date of 744 IP on Maintenance period is considered to be on Study Day 1 and the day before this is Study Day -1; i.e., there is no Study Day 0.

9.2.17. Long-Term Follow Up Study Day

The Long-Term Follow Up (LTFU) Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the last 744 IM injection, as follows:

if date of event > Last IM Injection, then

- LTFU Study Day = date of event - date of Last IM Injection

9.2.18. Extension Period Study Day

The Extension Period Study Day of an event (e.g., lab assessment, vital sign, ECG, start date of AE or HIV associated condition) will be derived as the number of days between the date of the event and the first IM injection (optimized Q8W/Q4W) for subjects in the Extension Switch Population (Section 6.1.13) as follows:

if date of event ≥ date of first injection, then

- Extension Period Study Day = date of event – first IM injection + 1

if date of event < start date of IP, then

- Extension Period Study Day = date of event – first IM injection

9.2.19. Total Cholesterol / HDL Cholesterol Ratio

When both total cholesterol and HDL cholesterol results are available from the same date for a subject, then the ratio will be calculated by dividing the total cholesterol result by the HDL cholesterol result.

9.3. Study Periods

AEs and concomitant medications will be assigned to study periods as defined in Table 14. Concomitant medications will be categorized as being concomitant within each treatment period as defined in Table 28 of Section 9.4.4.

Efficacy Assessments (HIV-1 RNA, CD4, HIV Associated Conditions, and Genotypic and Phenotypic Data) will be assigned to study periods as defined in Table 15

Laboratory Assessments, Vital Signs, and ECGs will be assigned to study periods as defined in Table 16.

In addition, all assessments/events will be assigned to the long-term follow up period as defined in Table 17.

Assessments/events are assigned to periods sequentially, starting from the top of each table. For example, if a subject does not participate in the maintenance period, then the date range for the Induction Period has no upper limit and all assessments with 'Date >= Induction Treatment Start date' (for Table 14) or Date > Induction Period Start Date (for Table 15 and Table 16) should be assigned to the Induction Period.

Examples:

- Maintenance Period Adverse Events:

  a) Q4W subject has injection at W96 and enters Extension period, with first extension phase injection at W100: AEs reported up to but not including date of W100 injection are assigned to the Maintenance Period

  b) Q4Wsubject has last injection at W44, withdraws from Maintenance period, and enters LTFU period; starts LTFU ART at LTFUM1 (28 days later): AEs reported up to but not including start of LTFU ART are assigned to the Maintenance Period

  c) Oral arm subject discontinues IP at Week 48 and has follow-up visit 30 days later: All AEs reported since the start of maintenance period IP are assigned to the Maintenance period, including AEs occurring post-treatment.

d) Oral arm subject completes maintenance and has first IM extension period injection at Week 100: AEs reported up to but not including date of W100 injection are assigned to the Maintenance Period.

- Maintenance Period Efficacy Assessments (Viral Load, CD4, HIV Associated Conditions, Virology):

a) Q4W subject has injection at W96 and enters Extension period, with first extension period injection at W100: HIV associated conditions with onset after Week 96 are excluded from Maintenance period, even if within 35 days of last maintenance injection;

b) Q4W subject has last injection at W44, withdraws from Maintenance period, and enters LTFU period: viral load collected at LTFUM1 (28 days since last injection) is excluded from Maintenance period, even though collection is within 35 days of last maintenance injection.

c) Oral arm subject completes maintenance and has first IM extension period injection at Week 100: viral load collected at Week 100 is excluded from the maintenance period.

Table 14 Assignment of Study Periods for AEs, Concomitant Medications

Study Period	Date range
Screen	Date < Induction Treatment Start Date
Induction	Induction Treatment Start Date ≤ Date < Maintenance Treatment Start Date
Maintenance	**Oral Randomized Arm:** Maintenance Treatment Start Date ≤ Date ≤ Date of First Extension Period IM injection – 1 or Withdrawn prior to Extension
	Q8W or Q4W Randomized Arms: **For subjects <u>not</u> receiving Extension Phase IP Injection:** Maintenance Treatment Start Date ≤ **Date** ≤ [max(Last Maintenance Period Injection Date + X [X=35 if last injection is Q4W, X=63 if last injection is Q8W], Date of Last Maintenance Period Oral Bridging Dose + 1)] <u>AND</u> **Date** < LTFU ART Start Date **For subjects receiving Extension Phase IP Injection:** Maintenance Treatment Start Date ≤ **Date** ≤ Date of First Extension Period IM injection – 1
Extension	Date of First Extension Period IM injection ≤ **Date** ≤ [Max(Date of Extension Loading Dose at Week 100 (if switching from oral arm to optimized Q4W) + 63, Last Extension Period Injection Date + X (X=35 days if last injection is Q4W, X=63 if last injection is Q8W), Date of Last Extension Period Oral Bridging Dose + 1)] <u>AND</u> **Date** < LTFU ART Start Date

- D**ate** = AE Start date/medication start date
- **Maintenance Treatment Start Date:** Date of first IM injection (i.e. Date of Day 1 IM Injection) for subjects randomized to maintenance IM regimen or start date of maintenance period investigational product for subject randomized to maintenance oral regimen.

Table 15 Assignment of Study Period for HIV-1 RNA, CD4, HIV Associated Conditions, and Genotypic and Phenotypic Data

Study Phase	Date range
Screen	Date ≤ Induction Treatment Start Date
Induction	Induction Treatment Start Date < Date ≤ Maintenance Treatment Start Date
Maintenance	Maintenance Treatment Start Date < Date ≤ min(Date subject failed to complete Maintenance Period [from Maintenance Period Conclusion form], Date of Week 96 Visit)
Extension	**If subject participating in the Extension Period:** min(Date subject failed to complete Maintenance Period [from Maintenance Phase Conclusion form], Date of Week 96 Visit) < Date ≤ min(Date subject failed to complete Extension Period [from Extension Phase Conclusion form], Date of Last Extension Phase Visit)
Follow-up	**If subject not participating in the Extension Period:** **Oral Randomized Arm:** Date > min(Date subject failed to complete Maintenance Period[from Maintenance Period Conclusion form], Date of Week 96 Visit)

- D**ate** = Assessment/start date
- **Maintenance Treatment Start Date:** Date of first IM injection (i.e. Date of Day 1 IM Injection) for subjects randomized to maintenance IM regimen or start date of maintenance phase study drug for subject randomized to the control arm.

Table 16 Assignment of Study Period for Laboratory Assessments, Vital Signs, and ECGs

Study Period	Date range
Screen	Date ≤ Induction Treatment Start Date
Induction	Induction Treatment Start Date < Date ≤ Maintenance Treatment Start Date
Maintenance	**Oral Randomized Arm:** Maintenance Treatment Start Date < Date ≤ Date of First Extension Period IM injection (expected to be Week 100 Injection) or Withdrawn prior to Extension Period
	Q4W or Q8W Randomized Arms: For subjects receiving Extension Period IP Injection: Maintenance Treatment Start Date < **Date** ≤ Date of First Extension Period IM injection (expected to be Week 100 for Q4W and Week 104 for Q8W). For subjects <u>not</u> receiving Extension Period IP Injection: Maintenance Treatment Start Date < **Date** ≤ min(LTFU ART Start Date, max[Last Maintenance Period Injection Date + X (X=35 days if last injection is Q4W, X=63 if last injection is Q8W), Date of Last Maintenance Period Oral Bridging Dose + 1])
Extension	Date of First Extension Period IM injection < **Date** ≤ min(LTFU ART Start Date, Max[Date of Extension Loading Dose at Week 100 (if switching from oral arm to optimized Q4W) + 63, Last Extension Period Injection Date + X (X=35 days if last injection is Q4W, X=63 if last injection is Q8W), Date of Last Extension Period Oral Bridging Dose + 1])

- **Date** = AE Start date

Maintenance Treatment Start Date: Date of first IM injection (i.e. Date of Day 1 IM Injection) for subjects randomized to maintenance IM regimen or start date of maintenance phase study drug for subject randomized to the control arm.

Table 17 Assignment to Long-Term Follow-Up Period

Study Period	Date range
Long-Term Follow-Up	Date > max(Last IM Injection Date, Last Oral Bridging End Date)

- Date = Assessment/Start Date
- If a subject withdraws during oral bridging, then the long-term follow up period is calculated using Date > Last IM Injection Date.

Note that the long-term follow-up period and maintenance/extension periods are not mutually exclusive by definition and are to be defined with separate period variables in the datasets. For example, an IM Q4W subject who has Week 92 injection and

withdrawal at Week 96 without receiving Week 96 injection, the "Week 96 withdrawal visit" belongs to both the maintenance period and long-term follow-up period.

9.3.1. Treatment State within Study Periods

Within each treatment study period (i.e. Induction, Maintenance, and Extension—after assignment of study period described in Section 9.3), only those assessments which occur within the ranges shown in Table 18 will be considered 'on-treatment' for the given period.

For adverse events, where a partial start date uses imputation as described in Section 9.1.6.2. In the case of a completely missing start date, the event will be considered to have started during induction treatment unless an end date for the AE is provided which is before start of investigational product; then, the AE is assigned as Pre-treatment.

Table 18 Treatment State within Study Periods

Study Period[a]	Treatment State	Date Range
Screen	Pre-treatment	All assessments/events within period
Induction	On-treatment	Date ≤ Induction Treatment Stop Date + 1
	Post-treatment	Date > Induction Treatment Stop Date + 1
Maintenance	On-treatment	Oral arm: Date ≤ Maintenance IP Stop Date + 1
		IM Q8W arm: Date ≤ max(Last Maintenance Injection Date + 63, Last Oral Bridging End Date + 1)
		IM Q4W arm: Date ≤ max(Date of IM Loading Dose at Day 1+ 63, Date of Last Q4W IM Dose + 35, Last Oral Bridging End Date + 1)
	Post-treatment	Oral arm: Date > IP Stop Date + 1
		IM Q8W arm: Date > max(Last Maintenance Injection Date + 63, Last Oral Bridging End Date + 1)
		IM Q4W arm: Date > max(Date of IM Loading Dose at Day 1+ 63, Date of Last Maintenance Q4W IM Dose + 35, Last Oral Bridging End Date + 1)
Extension	On-treatment	Q8W dosing for Extension (randomized IM Q8W arm or Oral arm switching to optimized IM Q8W): Date ≤ max(Last Extension Injection Date + 63, Last Oral Bridging End Date + 1)
		Q4W dosing for Extension (randomized IM Q4W arm or Oral arm switching to optimized IM Q4W):

Study Period[a]	Treatment State	Date Range
		Date ≤ max(Date of Extension Loading Dose at Week 100 (if switching from oral arm) + 63, Date of Last Extension Q4W IM Dose + 35, Last Oral Bridging End Date + 1).
	Post-treatment	Q8W dosing for Extension (randomized IM Q8W arm or Oral arm switching to optimized IM Q8W): Date > max(Last Extension Injection Date + 63, Last Oral Bridging End Date + 1)
		Q4W dosing for Extension (randomized IM Q4W arm or Oral arm switching to optimized IM Q4W): Date > max(Date of Extension Loading Dose at Week 100 (if switching from oral arm) + 63, Date of Last Extension Q4W IM Dose + 35, Last Oral Bridging End Date + 1).

- Note: Treatment State is determined after data has been assigned to the study periods as defined in Section 9.3.
- Date = Assessment/Start Date.

Table 19 Treatment State for LTFU Period data

Study Period[a]	Treatment State	Date Range
Long-Term Follow-up	On-treatment	If Last IM Regimen is Q8W: Date ≤ min(LTFU ART start date, max(Last Injection Date + 63, Last Oral Bridging End Date + 1))
		If Last IM Regimen is Q4W: Date ≤ min(LTFU ART start date, max(Date of Extension Loading Dose at Week 100 (if switching from oral arm to optimized Q4W) + 63, Last Injection Date + 35, Last Oral Bridging End Date + 1))
	Post-treatment	If Last IM Regimen is Q8W: Date > min(LTFU ART start date, max(Last Injection Date + 63, Last Oral Bridging End Date + 1))
		If Last IM Regimen is Q4W: Date > min(LTFU ART start date, max(Date of Extension Loading Dose at Week 100 (if switching from oral arm to optimized Q4W) + 63, Last Injection Date + 35, Last Oral Bridging End Date + 1))

a. Note: Treatment State is determined after data has been assigned to the study periods as defined in Section 9.3.

Date = Assessment/Start Date.

9.4. Assessment Windows

9.4.1. Assessment Window Assignment

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

In most cases the window around an assessment will include all dates from the midpoints between the target day and that of the previous and the proceeding visits, and, in general, the nominal target study day for week *w* is (7**w*)+1.

Assessments summarized for the ITT-E population (e.g. Day 1 analysis study report displays) are assigned as shown in Table 20 based on the Induction Period Study Day (see Section 9.2.15) and Study Day (see Section 9.2.16).

For parameters that are not scheduled to be assessed at particular visits, the all-inclusive windows defined in will still be used; however, data summaries will only report scheduled visits. 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., MSDF).

Table 20 Assessment Windows for Summary Induction Period Data for the ITT-E Population

Day of Assessment	Assessment Window	Target Induction Period Study Day of Window	Target Study Day of Window	Reporting Assessment Window
Induction Study Day <-4	Screen	-28		Screen
-3 ≤ Induction Study Day ≤ 1	Induction Day 1	1		Week -20
2 ≤ Induction Study Day ≤ 42	Induction Wk 4	29		Week -16
43 ≤ Induction Study Day ≤ 70	Induction Wk 8	57		Week -12
71 ≤ Induction Study Day ≤ 98	Induction Wk 12	85		Week -8
99 ≤ Induction Study Day ≤ 126	Induction Wk 16	113		Week -4
127 ≤ Induction Study Day ≤ min(Study Day of Last Induction Period Dose + 1, Study Day of First Maintenance Period Dose)	Induction Wk 20	141	1	Day 1
Induction Study Day > Study Day of Last Induction Period Dose + 1 and Subject did not participate in Maintenance period	Follow-up			Follow-up

For subjects participating in the maintenance period, induction/maintenance period assessments (based on period slotting defined in Section 9.3) are assigned as shown in Table 21.

Table 21 Assessment Windows for Summary of Induction Period and Maintenance Period Data

Day of Assessment	Assessment Window	Target Induction Period Study Day of Window	Target Study Day of Window	Reporting Assessment Window
Induction Study Day <-4	Screen	-28		Screen
-3 ≤ Induction Study Day ≤ 1	Induction Day 1	1		Week -20
2 ≤ Induction Study Day ≤ 42	Induction Wk 4	29		Week -16
43 ≤ Induction Study Day ≤ 70	Induction Wk 8	57		Week -12
71 ≤ Induction Study Day ≤ 98	Induction Wk 12	85		Week -8
99 ≤ Induction Study Day ≤ 126	Induction Wk 16	113		Week -4
127 ≤ Induction Study Day ≤ min(Study Day of Last Induction Period Dose + 1, Study Day of First Maintenance Period Dose)	Induction Wk 20	141	1	Day 1
2 ≤ Study Day ≤ 17	Week 1		8	Week 1
18 ≤ Study Day ≤ 42	Week 4		29	Week 4
43 ≤ Study Day ≤ 70	Week 8		57	Week 8
71 ≤ Study Day ≤ 98	Week 12		85	Week 12
99 ≤ Study Day ≤ 126	Week 16		113	Week 16
127 ≤ Study Day ≤ 154	Week 20		141	Week 20
155 ≤ Study Day ≤ 182	Week 24		169	Week 24
183 ≤ Study Day ≤ 210	Week 28		197	Week 28
211 ≤ Study Day ≤ 238	Week 32		225	Week 32
239 ≤ Study Day ≤ 266	Week 36		253	Week 36
267 ≤ Study Day ≤ 294	Week 40		281	Week 40
295 ≤ Study Day ≤ 322	Week 44		309	Week 44
323 ≤ Study Day ≤ 364	Week 48		337	Week 48
365 ≤ Study Day ≤ 420	Week 56		393	Week 56
421 ≤ Study Day ≤ 476	Week 64		449	Week 64
477 ≤ Study Day ≤ 532	Week 72		505	Week 72
533 ≤ Study Day ≤ 588	Week 80		561	Week 80
589 ≤ Study Day ≤ 644	Week 88		617	Week 88
645 ≤ Study Day ≤ 700	Week 96		673	Week 96
(7*w - 27) ≤ Study Day ≤ (7*w + 28)	Week w w = 104,112,etc.		7*w + 1	Week w w = 104,112,etc.

Day of Assessment	Assessment Window	Target Induction Period Study Day of Window	Target Study Day of Window	Reporting Assessment Window
If Last Dose of Study IP is Oral CAB: Date > (Date of Last Dose +1)	Follow-up			Follow-up
If Last Dose of Study IP is Q4W IM: Date > min(LTFU ART start date, max(Date of First IM Loading Dose at Day 1+ 63, Date of Week 100 Loading Dose [subjects switching from oral to optimized Q4W], Last Injection Date + 35, Last Oral Bridging End Date + 1))				
If Last Dose of Study IP is Q8W IM: Date > min(LTFU ART start date, max(Last Injection Date + 63, Last Oral Bridging End Date + 1))				

Extension period assessments (based on period slotting defined in Section 9.3) are assigned as shown in Table 22 and Table 23.

Table 22 Assessment Windows for Extension Period Data: Subjects Continuing Randomized Q4W/Q8W IM Regimen

Day of Assessment	Assessment Window	Target Extension Period Study Day of Window
687≤ Study Day ≤714	Week 100	701
715≤ Study Day ≤742	Week 104	729
743≤ Study Day ≤770	Week 108	757
771≤ Study Day ≤ 840	Week 112	785
841≤ Study Day ≤952	Week 128	897
953≤ Study Day ≤1064	Week 144	1009
(7*w - 55) ≤ Study Day ≤ (7*w + 56)	Week w w = 160, 176,…	7*w + 1

Table 23 Assessment Windows for Extension Period Data: Subjects Switching from Randomized Oral Regimen to Optimized Q8W/Q4W IM Dosing

Day of Assessment	Assessment Window	Target Extension Period Study Day of Window	Reporting Assessment Window
Extension Study Day ≤1	Day 1	1	Week 100
2 ≤ Extension Study Day ≤ 17	Week 1	8	Week 101
18 ≤ Extension Study Day ≤ 42	Week 4	29	Week 104
43 ≤ Extension Study Day ≤ 70	Week 8	57	Week 108
71 ≤ Extension Study Day ≤ 98	Week 12	85	Week 112
99 ≤ Extension Study Day ≤ 126	Week 16	113	Week 116
127 ≤ Extension Study Day ≤ 154	Week 20	141	Week 120
155 ≤ Extension Study Day ≤ 182	Week 24	169	Week 124
183 ≤ Extension Study Day ≤ 252	Week 28	197	Week 128
253 ≤ Extension Study Day ≤ 364	Week 44	309	Week 144
(7*w - 55) ≤ Extension Study Day ≤ (7*w + 56)	Week w w = 60,76,…	7*w + 1	Week (w + 100)
If Last Dose of Study IP is Q4W IM: Date > min(LTFU ART start date, max(Date of Extension Loading Dose at Week 100 (if switching from oral arm to optimized Q4W) + 63, Last Injection Date + 35, Last Oral Bridging End Date + 1))	Follow-up		Follow-up
If Last Dose of Study IP is Q8W IM: Date > min(LTFU ART start date, max(Last Injection Date + 63, Last Oral Bridging End Date + 1))			

Assessment windows for the purposes of the Snaphot(MSDF) algorithm are defined in Table 24 based on data assigned to the maintenance period as defined in Section 9.3)

Table 24 Expanded Assessment Windows for Summary of Snapshot (MSDF) Data (Window at Key Analysis Time points) - Data in Maintenance Period Only

Day of Assessment	Reporting Assessment Window	Snapshot Windows
211 ≤ Study Day ≤ 238 or 183 ≤ Study Day ≤ 266	Week 32	±2 Week, if no data in the window, expand window to ± 6 week
323 ≤ Study Day ≤ 364 or 295 ≤ Study Day ≤ 378	Week 48	-2 and +4 Week, if no data in the window, expand window to ± 6 week
631 ≤ Study Day ≤ 714	Week 96	± 6 Week
> Study Day of max[Last Maintenance Q4W IM Injection + 35, Last Maintenance Q8W IM Injection + 63, min(Maintenance Oral Stop Date +1, Week 96 Visit in eCRF)]	Not Evaluable	

Assessments in the LTFU period will be assigned to assessment windows as shown in Table 25.

Table 25 Assessment Windows for Summaries of Long-Term Follow Up Period Data

Day of Assessment	Assessment Window	Target Induction Period Study Day of Window	Target Study Day of Window
1 ≤ LTFU Study Day ≤ 60	Month 1		30
61 ≤ LTFU Study Day ≤ 135	Month 3		90
136 ≤ LTFU Study Day ≤ 225	Month 6		180
226 ≤ LTFU Study Day ≤ 315	Month 9		270
316 ≤ LTFU Study Day ≤ 405	Month 12		360
(30*m - 44) ≤ LTFU Study Day≤ (30*m + 45)	Month m m = 15, 18, ...		30*m

Assessment windows for the purposes of the Snapshot(MSDF) algorithm for the Extension Switch population are defined in Table 26 based on data assigned to the Extension period as defined in Section 9.3).

Table 26 Assessment Windows for Summary of Snapshot (MSDF) Data (Window at Key Analysis Time points) — Subjects Switching from Randomized Oral Regimen to Optimized Q8W/Q4W IM Dosing (Data in Extension Period Only)

Day of Assessment	Assessment Window	Snapshot Windows	Reporting Assessment Window
155 ≤ Extension Study Day ≤ 238	Week 28	± 6 Week	Week 128
379 ≤ Extension Study Day ≤ 462	Week 60	± 6 Week	Week 160
> Extension Study Day of max[Last Extension Q4W IM Injection + 35, Last Extension Q8W IM Injection + 63]	Not Evaluable		

Table 27 Assessment Windows for Summary of Snapshot (MSDF) Data (Window at Key Analysis Time points) — Randomized Subjects Who Continued Q8W/Q4W IM Dosing during the Extension Period

Day of Assessment	Reporting Assessment Window	Snapshot Windows
1079 ≤ Study Day ≤ 1162	Week 160	± 6 Weeks
> Study Day of max[Last Extension Q4W IM Injection + 35, Last Extension Q8W IM Injection + 63, Week 160 Visit in eCRF)]	Not Evaluable	

*Study day = maintenance study day

9.4.2. Multiple Assessments

If after window assignment there are multiple valid (see Section 9.4.3) 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:

1. the assessment closest to the window target Study/Induction/LTFU Day;
2. if there are multiple assessments equidistant from the target day, then the mean of these values will be used.

Except for HIV-1 RNA and laboratory data which will be handled differently depending on the method being used to analyse the data. As stated in Section 9.2.10, if multiple assessments are collected during the analysis window, then the last on-treatment assessment in that window will be used for calculating the Snapshot/MSDF outcome. For OC, HIV-1 RNA data as a continuous measure, and laboratory data, if more than one assessment was collected during the scheduled visit window, then the closest on-treatment assessment to the scheduled visit will be used. If two assessments are equidistance and closest to the scheduled visit, then the later of the two assessments collected will be used.

Assessments not chosen for use in summary statistics by this algorithm will still appear in the associated listings.

9.4.3. Invalid Laboratory Assessments

Certain laboratory endpoints are required to be collected in a fasting state: glucose, and lipids (triglycerides, total cholesterol, HDL, LDL). If these endpoints are collected in a non-fasting state, then the results will be excluded from summaries; such results will be included in data listings with the fasting status noted.

9.4.4. Classification of Prior, Concomitant, and Post-Therapy Medications

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

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

Table 28 illustrates how a medication is classified as prior, concomitant, or post-treatment.

Table 28 Prior, Concomitant, and Post-treatment Classification of Medications

	Pre-treatment	On-treatment			Post-treatment		Prior	Concomitant	Post
		Induction IP Start Date		End of on-treatment window [a]					
(a)	x————x						Y	N	N
(b)	x————		————x				Y	Y	N
(c)	x————		————			————x	Y	Y	Y
(d)			x————x				N	Y	N
(e)			x————			————x	N	Y	Y
(f)						x————x	N	N	Y
(g)	?————x						Y	N	N
(h)	?————		————x				Y*	Y	N
(i)	?————		————			————x	Y*	Y*	Y
(j)	x————		————			————?	Y	Y**	Y**
(k)			x————			————?	N	Y	Y**
(l)						x————?	N	N	Y
(m)	?————		————			————?	Y***	Y***	Y***
(n)	x————	x					Y	Y	N
(o)	?————	x					Y	Y	N
(p)		x	————x				N	Y	N
(q)		x	————	x			N	Y	N
(r)				x	—	————x	N	Y	Y
(s)				x	—	————?	N	Y	Y
(t)					x	————x	N	N	Y
(u)					x	————?	N	N	Y
(v)			x————	—	x		N	Y	Y

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

a. End of on-treatment window:
   - Oral arm: max(Induction Treatment Stop Date + 1, Maintenance IP Stop Date + 1, Last Extension Period Injection Date + X (X=35 days if last injection is optimized Q4W, X=63 if last injection is optimized Q8W, Last Oral Bridging End Date + 1)
   - IM Q8W arm: max(Induction Treatment Stop Date + 1, Last Injection Date + 63, Last Oral Bridging End Date + 1)
   - IM Q4W arm: max(Induction Treatment Stop Date + 1, Date of IM Loading Dose at Day 1+ 63, Date of Last Q4W IM Dose + 35, Last Oral Bridging End Date + 1)

Concomitant medications (as defined above) will be further categorized as being concomitant during Induction, Maintenance, and Extension period, respectively, according to whether the medication was taken between the following time points:

Concomitant during:	**Date range**
Induction	Induction Treatment Start Date ≤ **Medication Taken** < Maintenance Treatment Start Date
Maintenance	**Oral Randomized Arm:** Maintenance Treatment Start Date ≤ **Medication Taken** ≤ Date of First Extension Period IM injection – 1 or Withdrawn prior to Extension
	Q8W or Q4W Randomized Arms: **For subjects <u>not</u> receiving Extension Phase IP Injection:** Maintenance Treatment Start Date ≤ **Medication Taken** ≤ max(Last Maintenance Period Injection Date + X [X=35 if last injection is Q4W, X=63 if last injection is Q8W], Date of Last Maintenance Period Oral Bridging Dose + 1) <u>AND</u> **Date** < LTFU ART Start Date **For subjects receiving Extension Phase IP Injection:** Maintenance Treatment Start Date ≤ **Medication Taken** ≤ Date of First Extension Period IM injection – 1
Extension	Date of First Extension Period IM injection ≤ **Medication Taken** ≤ [Max(Date of Extension Loading Dose at Week 100 (if switching from oral arm to optimized Q4W) + 63, Last Extension Period Injection Date + X (X=35 days if last injection is Q4W, X=63 if last injection is Q8W), Date of Last Extension Period Oral Bridging Dose + 1)] <u>AND</u> **Date** < LTFU ART Start Date

If a partial date is recorded in the eCRF, the following convention will be used to assign the medication:

- if the partial date is a start date, a '01' will be used for missing days and 'Jan' will be used for missing months;
- if the partial date is a stop date, a '28/29/30/31' will be used for the missing day (dependent on the month and year) and 'Dec' will be used for the missing month; for medications recorded separately in the eCRF as prior ART, the earlier of this imputed date or the day before IP start will be used.

The recorded partial date will be displayed in listings.

9.5. Values of Potential Clinical Importance

The DAIDS grading for severity of laboratory toxicities and clinical adverse events is included in the protocol (Appendix 2). The central laboratory will flag lab parameter toxicities directly in the provided datasets.

10. STUDY POPULATION

For the Day 1 interim analysis, all displays referred to in this section will be presented for the ITT-ME population, unless otherwise indicated.

For the Week 96 study report, all displays referred to in this section will be presented for the ITT-ME population, unless otherwise indicated. Data displays using other populations will be detailed in Section 17.2.

For the Week 128 study report, all displays referred to in this section will be presented for the Extension Switch population, unless otherwise indicated.

Starting from RAP amendment #3, certain data summary and data listing displays have been updated or added to align with recent updates to IDSL data display standards. These changes are indicated in the table of contents of Section 17.2.2.

10.1. Disposition of Subjects

The total number of subjects in each analysis population will be summarized and a listing will present which populations each subject belonged to. The number and percentage of subjects who failed screening will be summarized by reason for failure. A listing will show subjects screened but not enrolled, along with the reason for discontinuation at this stage. A listing will also be produced to show any subjects enrolled but who did not receive investigational product.

The treatment number assigned and the corresponding treatment, for all subjects, will be listed by country and site number. A listing of subject numbers and randomization numbers with assigned and actual randomization strata, treatment assignment, and start date of randomized treatment will be presented. This listing will be ordered by country, site, and subject number and will also show the investigator name for each subject.

A summary of subject disposition, i.e., the number and percentage of subjects who enrolled in and completed each period (e.g, Induction, Maintenance, Extension and long-term follow-up) of the study, as well as subjects who withdrew from the study as recorded in the eCRF Phase Conclusions pages. A subject is considered to have completed the study if they did not prematurely discontinue IP prior to Week 96. Subjects who have not been recorded as either completing or withdrawing from the study will be categorized as "Ongoing at time of the analysis" for summary purposes. Listings of investigational product discontinuation and subject disposition will be provided.

10.2. Protocol Deviations

10.2.1. Inclusion / Exclusion Criteria

A listing of subjects and the criteria they deviated from will be produced.

10.2.2. Important Protocol Deviations

The number and percentage of subjects with important protocol deviations will be summarized by treatment group and overall. A listing of subjects and their important protocol deviations will be produced.

10.2.3. Important Protocol Deviations that exclude subject from Per protocol population

Important protocol deviations leading to exclusion from Per Protocol population are those deviations which may

i. directly impact the efficacy endpoint of HIV-1 RNA; or

ii. lead to permanent discontinuation of IP/withdrawal and hence indirectly impact the efficacy endpoint by causing data to be missing.

The following criteria define the protocol deviations which, if they occur prior to an analysis time point of interest, will lead to exclusion of a subject from the Per-Protocol population for that analysis. Potential protocol deviations leading to exclusion from PP population will be reviewed by the study team to confirm that they meet these criteria. This review will occur before the clinical database has been frozen for analysis. The review process will be conducted at the primary and interim analyses (Day 1, Weeks 32, 48, 96, 128 and 160).

- Subject deviates from any inclusion or exclusion criteria, as recorded on the eCRF Eligibility Question form;
- Subject has non-compliance with investigational product or took/received incorrect IP (i.e., other than the one to which they were randomized) for greater than 10% of total time on-treatment (shown in Table 29) up to an analysis time point visit of interest.

Table 29 Total Time On-Treatment for the Calculation of Dosing Non-Compliance/Incorrect Investigational Product at Each Analysis Time Point

Population	Treatment Arms	Analysis Time Point	Total Time On-Treatment
ITT-ME	Oral and Randomized IM	Week 32, Week 48 and Week 96	Total time in the Maintenance period up to the analysis time point
Extension Switch Population[a]	Optimized Q8W and Optimized Q4W	Week 128 and Week 160	Total time in the Extension period up to the analysis time point
ITT-ME	Randomized IM	Week 160	Total time in the Maintenance + Extension period up to Week 160

- For this purpose, the **total number of non-compliant dosing days** up to the analysis timepoint visit (or date of IP discontinuation/maintenance period withdrawal, whichever is earlier), is derived as follows:
  - Oral Arm: Interruptions of oral 744 for reasons other than treatment-related adverse events/laboratory abnormalities, based on eCRF IP Dosing forms;
  - IM arm: Time until next injection from the occurrence of any of the following (summing across all injections):
    - Date of Projected Injection Visit + 7 days, if injection received >7 days from projected injection visit date (without bridging) with the exception for the W104 and W108 visits for the Extension Switch population[b];
    - Date of Dosage/administration deviation potentially resulting in under dosage + 7 days;
    - Date of Dosage/administration deviation potentially resulting in over dosage.

a. For the Extension Switch population at analysis time points Week 128 and Week 160, only non-compliant dosing days during the Extension Period will be counted.

b. For the Extension Switch population, the second injection should occur within 3 to 4 weeks after the first loading dose at W100. In addition, for the Optimized Q4W subjects, the third injection should occur within the window of 7 to 8 weeks relative to the first loading dose. Therefore, the +7 dosing window is not allowed for these time points, and therefore the non-compliant time until next injection should be calculated directly from the projected injection visit. For example, if a W108 injection is late by 2 days from the projected W108 visit, then the number of non-compliant dosing days equals 2.

- Prohibited medications prior to primary timepoint: receiving ART medication other than that prescribed by the study or receiving non-ART medication that would impact IP or NRTI backbone exposure or response to therapy. The clinical team will review the listing of unique concomitant medication terms before database freeze and select the prohibited medications (with duration and timing of use taken into account as appropriate);
- Oral arm: Switch of NRTI backbone for reason other than toxicity management or more than 1 switch of NRTI backbone during the first 96 weeks maintenance period of the study prior to a specified analysis timepoint;
- Study withdrawal due to a reason of "Protocol Deviation" (as recorded in the eCRF) prior to a specified analysis timepoint.
- Other important protocol deviations that exclude subject from Per protocol population as recorded in the study team Protocol deviation review documents.

The number and percentage of subjects with important protocol deviations that exclude subject from Per protocol population will be summarized by treatment group and overall.

10.3. Demographic and Baseline Characteristics

Demographic characteristics (gender, age, age categories, and ethnicity) collected at screening, height at baseline BMI at Day 1 will be summarized. Date of birth, the screening assessment date, age, gender, and ethnicity will be included in the listing of demographic data.

The five high level FDA race categories and designated Asian subcategories will be summarized along with all combinations of high level categories which exist in the data. The nine race categories collected will be summarized along with categories for mixed race. A by-subject listing of race will also be produced.

Baseline Hepatitis B and C status will also be summarized and all Hepatitis B and C results will be listed.

Numbers and percentages of subjects with CDC Classification of HIV Infection categories A, B, and C at baseline will be summarized and listed. HIV risk factor/mode of transmission will be summarized and listed.

Current and past medical conditions at Baseline will be summarized separately, for each treatment group and overall. All past and current conditions will be listed. Medical conditions will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).

A summary of cardiovascular risk assessments will be produced. The number and percentages of subjects with family cardiac history (parent or sibling with heart attack or stroke before age 55) and subjects' smoking history (never, current, former) at Baseline will be presented; smoking history at time of withdrawal will also be included. The summary will also include a 10-year risk of coronary heart disease, as calculated using Baseline values in the Framingham equation (see Section 9.2.5); summary statistics will

be presented along with the number and percentage of subjects with <10%, 10% to <20%, and ≥20% risk. A listing of data related to cardiovascular risk assessments will be produced.

The distribution of plasma HIV-1 RNA at Screening and Baseline will be summarized. This will include the number and percentage of subjects with plasma HIV-1 RNA (c/mL) in the categories specified in Section 8.3, as well as summary statistics of $\log_{10}$ c/mL values. A similar summary will be produced for CD4+ cell count data (cells/mm^3). Listings of HIV-1 RNA and CD4+ values will be included in efficacy outputs.

10.3.1. Associations between Baseline Characteristics

To explore associations between baseline characteristics, cross-tabulations of certain subgroups from Section 8.3 may be performed if there are sufficient number of patients in the subgroups. The number and percentage of subjects in each combination of categories from the following pairs of subgroups will be summarized:

10.4. Treatment Compliance

A listing of dispensation information (dates and number of tablets dispensed and returned) will be produced.

10.5. Concomitant Medications

For reporting purposes, medications will be classified as prior, concomitant, and/or post-treatment using the associated start and stop dates recorded in the eCRF and relative to the first and last dose dates of investigational product (see Section 9.4.4). Medications will be coded using the GSK Drug coding dictionary.

Concomitant medications will be summarized by GSK-Drug Anatomical Therapeutic Chemical (ATC) classification level 1 (body system). Drugs will be displayed according to the ATC classifications of both their ingredient and combination term. The data will also be summarized by ingredient combinations alone.

A summary of the number and percentage of subjects receiving concomitant medications will also be displayed using a method that presents multi-ingredient medications according to their combination ATC classification rather than the classifications of the ingredients. This display will also include single-ingredient medications. Multi-ingredient medications will be labelled according to the sum of their ingredients, e.g., “Tylenol Cold and Flu” would appear as “CHLORPHENAMINE MALEATE + DEXTROMETHORPHAN HYDROBROMIDE + PARACETAMOL + PSEUDOEPHEDRINE HYDROCHLORIDE” under the ATC headings for “Nervous System” and “Respiratory System” (the combination’s ATC classifications).

A listing of all medications taken by subjects, including any which are only prior or post-treatment, will be produced. The relationship between ATC level 1, ingredients and verbatim text for all medications in the study will be listed.

10.6. Prior and Concomitant ART

ART medications will also be classified as prior, concomitant, and/or post-treatment according to Section 9.4.4, with the modification that **starting on IP stop date will be considered as only post-treatment and not concomitant**. It is expected that after discontinuation of IP, a subject may immediately begin taking another ART. Also, any ART entered on the Prior ART eCRF with partial end date will be assumed to have finished before Screening.

All summaries of concomitant ART will be presented by treatment group and will be summarized by GSK Drug ATC classification level 4 (which will provide ART class) and ingredient.

Concomitant ART at Baseline (i.e., selected background NRTI) will be summarized by treatment group. Details of any prior ART, since this is a naïve treatment population this is expected to be minimal, will be listed separately. A listing will be produced for concomitant and **Post-treatment ART, with an additional listing for subjects receiving more than one concomitant ART** (i.e., to identify subjects who switched background therapy during the study). The hierarchical relationship between the ATC level 4, combination term, and verbatim text will be listed.

11. EFFICACY ANALYSES

For the Day 1 interim analysis, efficacy analyses will be based on the ITT-E population.

For the Week 32/48/96 analyses, efficacy analyses will be based on the ITT-ME population, unless stated otherwise.Efficacy data displays for the Week 96 analysis report will generally only use data from the Induction and/or Maintenance Period (i.e. up to Week 96); limited data displays will be produced including Extension Period data since this data will be more thoroughly investigated in future planned study reports (i.e. Week 128 and Week 160analyses). Refer to Section 17.2.2 for specification of which displays will include Extension period data.

For the Week 96 analysis, listings will present all available data, including from the Extension period which may not be summarized until future study reports. Listings will present data grouped according to the expanded treatment sequence arms of Table 8.

Starting from RAP amendment #3, certain data summary and data listings displays have been updated or added to a) include extension period data, and b) to align with recent updates to IDSL data display standards. These changes are indicated in the table of contents of Section 17.2.2.

For the Week 128 analysis, efficacy analyses will be based on the Extension Switch Population, unless otherwise noted. Data displays will generally only use data from the Extension Period up to Week 128.

For the Week 160 analysis, efficacy analyses will be summarized in separate displays for the "Randomized Q8W/Q4W IM" and the Extension Switch Population. Listings will present data grouped according to the expanded treatment sequence arms of Table 8.

11.1. Primary Efficacy Analysis: Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL

The primary efficacy endpoint is the proportion of subjects with HIV-1 RNA <50 c/mL at Week 32/48 using the MSDF (Snapshot) algorithm (see Section 9.2.10). The ITT-ME population will be the primary population for primary efficacy analysis.

11.1.1. Summaries

The number and proportion of subjects with plasma HIV-1 RNA level below 50 c/mL at the time of analysis based on the MSDF algorithm will be summarised by treatment group.

A summary of study outcomes (i.e., response below 50 c/mL or reason for no data in the window) at the time of analysis (e.g., Day 1, Week 32/48/96), based on the MSDF algorithm, will be presented by treatment. Unadjusted difference in proportions between each of IM arm vs oral arm and corresponding two-sided 95% CI will also be presented. Study outcomes will also be listed.

In addition, the number and proportion of subjects with plasma HIV-1 RNA level below 50 c/mL based on the MSDF algorithm will be summarized by treatment group for each visit. Line plots, with 95% confidence intervals for the proportion of subjects below 50 c/mL by treatment group at each visit, will be produced.

To assess the impact of important protocol deviations that exclude subjects from the per protocol population, the summary of responders below 50 c/mL at the time of analysis (e.g., Day 1, Week 32/48/96) will be repeated using the PP-ME populations.

11.1.2. Main Analysis

The ITT-ME population will be used for the main analysis.

For the analysis of GSK744 LA+TMC278 LA arms (IM arms) response rate relative to GSK744 + ABC/3TC (oral arm), let:

X_{IM} = number of responder in IM arm, and

X_{oral} = number of responder in oral arm

The binomial distribution is the assumed likelihood of the response data, as follows:

$$X_{IM} \sim \text{Binomial}(90, p_{IM})$$

$$X_{oral} \sim \text{Binomial}(45, p_{oral})$$

Since the true response rate is unknown, prior distributions are placed on these parameters of interest to reflect current beliefs and balanced with acceptable decision criteria performance. Conjugate beta densities are assumed. The information pertaining to the oral arm response rate is well understood and the prior that was chosen reflects the belief that the response rate is between 78% and 99% with 95% certainty. There is very few information about the response rate for IM arm, therefore, a non-informative prior assumed.

$P_{IM} \sim$ Beta (1, 1)

$P_{oral} \sim$ Beta (23, 2)

The posterior probability that the response rate for IM arm demonstrates the comparability of oral arm is as follows:

$p_1 = P (P_{IM} > p_{oral} - 0.1 \mid \text{data})$

A posterior probability of at least 90% (i.e., $p_1 > 0.90$) corresponds to "substantial evidence of positive outcome" and is chosen as the weight of evidence threshold.

Sensitivity analyses may be performed to assess the impact of the choice of informative prior for oral arm response rate though the analysis described above will remain primary for indication of efficacy decision-making purposes. As an alternative to the informative prior, a Beta (1, 1) prior distribution for oral arm may be considered.

11.2. Secondary Efficacy Analyses

11.2.1. Proportion of Subjects with Plasma HIV-1 RNA <200 c/mL

The outputs detailed in Section 11.1 will also be produced using a responder threshold of <200 c/mL.

11.2.2. Observed Values and Change from Baseline in Plasma HIV-1 RNA (log_{10} c/mL)

The observed values and changes from baseline in plasma HIV-1 RNA (log_{10} copies/mL) by week will be presented in summary tables. The data will be listed and profile plots of each individual's observed values will be produced.

11.2.3. Observed Values and Change from Baseline in CD4+ and CD8+ Cell Counts

The observed values and changes from baseline in CD4+ cell count (cells/mm^3) by week will be presented in summary tables as well as listed. The observed values and changes from baseline in CD8+ cell count (cells/mm^3) by week will be presented in summary tables and listings. The CD4+/CD8+ cell count ratio will be listed.

11.2.4. Virologic Failure

The cumulative proportion of subjects with protocol-defined virologic failure will be summarised by visit in terms of virologic non-response, virologic rebound and overall. The distribution of quantitative plasma HIV-1 RNA results at the time of suspected and confirmation of PDVF will be summarised by treatment group.

A listing of PDVF subjects will be provided. This will identify the visit of failure, type of PDVF(rebound or non-response) and study phase of the confirmation result (Induction , Maintenance or Extension).

11.2.5. Virologic or Tolerability Failure

The proportion of subjects without virologic or tolerability failure by the analysis timepoint (Week 32/48/96) will be estimated using the Kaplan-Meier nonparametric method based on the time to protocol defined virologic failure (PDVF) or treatment related/efficacy related discontinuation (i.e., drug-related AE/intolerability of injections, protocol defined safety stopping criteria, or lack of efficacy). Subjects who have not met PDVF criteria and are ongoing in the study, or who have discontinued for reasons other than those related to treatment during the maintenance period, will be censored.

The estimated proportion without failure at the time of analysis (Week 32/48/96) will be presented for each treatment group. The estimated difference in proportion for each IM arm relative to the Oral 744 arm will also be presented, along with its associated two-sided 95% CI.

The estimate of the standard error used to derive confidence intervals for the difference in proportions between treatment groups will be based on Greenwood's formula [Kalbfleisch, 1980].

Kaplan-Meier Plots for time to virologic or tolerability failure will be provided for each treatment group for the maintenance period.

11.2.6. HIV Associated Conditions

A summary of maintenance period HIV associated conditions, including those which are a recurrence of a previous condition, will be presented. The summary will be repeated excluding those HIV associated conditions which are a recurrence of a previous condition. All data will be included in a listing.

11.2.7. HIV Disease Progression

The number and proportion of subjects experiencing clinical disease progression or death during the maintenance period will be presented, with clinical disease progression defined as the progression from baseline HIV disease status as follows:

- CDC Category A at baseline to CDC Category B event

- CDC Category A at baseline to CDC Category C event
- CDC Category B at baseline to CDC Category C event
- CDC Category C at baseline to new CDC Category C event
- CDC Category A, B or C at baseline to death

11.2.8. Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL: Q8W vs. Q4W

The comparability between the IM dosing arms in terms of the proportion of subjects with plasma HIV-1 RNA level below 50 c/mL at the time of analysis (Week 32/48) based on the MSDF algorithm will be assessed using the Bayesian probability model described in Section 7.2. The posterior probability for comparability, based on an equivalence criterion, P2=P ($|PQ_{8W} - PQ_{4W}| < 0.1$ | data), will be provided.

A posterior probability of at least 90% (i.e., P2 >0.90) corresponds to "substantial evidence of positive outcome" and is chosen as the weight of evidence threshold for concluding that the two IM dosing regimens are equivalent.

11.3. Other Efficacy Analyses

The summary of the proportion of subjects who were responders at the analysis timepoint (Week 32, 48 and 96) based on the MSDF algorithm of those subjects in the ITT-ME population that first suppressed (<50 c/mL) at Week -4, -8, -12, -16, separately, will be presented by treatment group. The effect of the time to first HIV-1 RNA suppression in the Induction period on the response during the Maintenance period may be explored using logistic regression including baseline and/or PK covariates in the model.

The summary of the proportion of subjects with plasma HIV-1 RNA level below 50 copies/mL, using the MSDF algorithm, by treatment group and visit will be repeated for certain subgroups, as described in Section 8.3.

The summary of study outcomes at the time of analysis may also be produced for certain subgroups, as described in Section 8.3.

A listing of those subjects that switched background NRTIs during the study will provide the duration on NRTI, visit and date of switch, what the subject switched to and reason for switch.

A listing of quantitative plasma HIV-1 RNA data for subjects classified as having 'data in window >50' at any maintenance period visit based on the Snapshot (MSDF) classification will be provided.

A listing of quantitative plasma HIV-1 RNA data for subjects with HIV-1 RNA ≥ 50 c/mL at any time during the Maintenance Period or Extension Period will be provided. Line plots, with 95% confidence intervals, for the proportion of subjects with virologic failure over time for each treatment group based on the Snapshot (MSDF) algorithm (HIV-1 RNA threshold of 50 c/mL) will be produced.

The summary of the proportion of subjects with plasma HIV-1 RNA level below 50 copies/mL, using an observed case dataset, by treatment group and visit will be produced.

11.3.1. Exploratory Analyses

The number and proportion of subjects with plasma HIV-1 RNA < 2 copies/mL according to the BIOMNTR low-level assay will be summarized by treatment group for each visit using the observe case method (see Section 9.1.1.2). A listing of BIOMNTR viral load results will also be produced.

For the Extension Period Analyses at Week 128 and Week 160, proportion of subjects with a 'virologic failure' endpoint, as well as the proportion of subjects with plasma HIV-1 RNA< 50 copies/mL per the FDA MSDF snapshot algorithm will be provided. Proportion of subjects with protocol defined virologic failures over time, proportion of subjects with plasma HIV-1 RNA < 200 c/mL and <50 c/mL over time, and the absolute values and changes in CD4+ cell counts over time will also be produced.

12. SAFETY ANALYSES

Safety displays of induction period data only will use the Safety Population, and all other safety displays for Week 32, Week 64 and Week 96 will use the Safety Maintenance Population, unless otherwise specified. For the Week 128 safety displays, the Extension Switch Population will be used. For the Week 128 safety displays, the Safety Maintenance population and the Extension Switch Population will be used.

In general, data displays for the Week 96 analysis report will use data from the Induction and/or Maintenance Period (i.e. up to Week 96). However, a limited set of additional safety displays will be generated to include Extension period data as follows:

- Combined time period of Induction and Maintenance Periods for subjects originally randomized to Q8W/Q4W IM maintenance regimens;
- Combined time period Maintenance Period plus Extension period for subjects originally randomized to Q8W/Q4W IM maintenance regimens;
- Extension period data only for subjects switching from the oral maintenance regimen to an optimized Q8W/Q4W IM for the extension period of the study.

Listings will present all available data, including from the Extension period which may not be summarized until future study reports. Listings will present data grouped according to the expanded treatment sequence arms of Table 8.

In general, data displays for the Week 128 analysis report will use data from the Extension Period (i.e. up to Week 128). Summaries will be produced by the "Optimized Q8W IM" and the "Optimized Q4W IM" treatment arms. Listings will in general only present available data within the Extension Period for the Extension Switch Population.

For the W160 safety analysis, the Safety Maintenance population (Q8W/Q4W IM) and the Extension Switch population will be summarized in separate displays unless otherwise noted. In general, maintenance period data for the randomized oral arm will not be repeated in the W160 analysis. Listings will present data grouped according to the expanded treatment sequence arms of Table 8 unless otherwise noted.

12.1. Extent of Exposure

The first and last doses and any changes/interruptions in dosing for oral regimen and dates of injections for IM arms will be listed for all subjects, together with details of the reason for any dose change/interruption. A separate listing will be generated for subjects receiving oral bridging.

Distribution and summary statistics for the duration of exposure to IP (defined in Section 9.2.4) will be presented.

12.2. Adverse Events

Adverse events will be coded using the most recent MedDRA coding dictionary to give a preferred term and a system organ class. These preferred terms and system organ classes will be used when summarising the data. The verbatim text will be used in listings together with the preferred term. A listing of the relationship of preferred term to verbatim text will be presented ordered by system organ class.

An AE will be counted in the study period corresponding to the onset date of the event (see Section 9.3).

Post-baseline events—including both on-treatment and post-treatment events as defined in Section 9.3.1—will be summarized separately for the induction period and induction plus maintenance periods combined. Maintenance period specific tables will summarize on-treatment events only. See Section 17.1.3 and Section 17.2.3 for details of AE summaries by period and population.

For displays of injection site reaction adverse events, common events will include pain, erythema, nodules and any other ISR with greater or equal to five percent of subjects.

The following adverse event summaries will be tabulated by treatment group:

1. All AEs by system organ class (SOC) (Induction + Maintenance: Post-baseline; Extension: On-treatment);
2. Common Non-Serious Adverse Events by SOC (Induction + Maintenance: Post-baseline; Extension: On-treatment; Maintenance + Extension: on-treatment)
3. Summary of Subjects and Number of Occurrences of Common Non-Serious Adverse Events by SOC (Induction + Maintenance: Post-baseline; Extension: On-treatment)
4. All AEs by overall frequency (Induction + Maintenance: Post-baseline; Induction: Post-baseline; Maintenance: On-treatment; Extension: On-treatment; Maintenance + Extension: on-treatment) ;

5. All AEs by SOC and maximum toxicity (Induction + Maintenance: Post-baseline; Induction: Post-baseline; Maintenance: On-treatment; Extension: On-treatment; Maintenance + Extension: on-treatment) ;
6. All grade 2-4 AEs by overall frequency(Induction + Maintenance: Post-baseline; Extension: On-treatment; Maintenance + Extension: on-treatment);
7. All drug-related AEs by overall frequency(Induction + Maintenance: Post-baseline; Extension: On-treatment; Maintenance + Extension: on-treatment);
8. All drug-related AEs by SOC and maximum toxicity (Induction + Maintenance: Post-baseline; Induction: Post-baseline; Maintenance: On-treatment; Extension: On-treatment; Maintenance + Extension: on-treatment) ;
9. All grade 3-4 drug-related AEs by overall frequency (Induction + Maintenance: Post-baseline; Induction: Post-baseline; Maintenance: On-treatment; Extension: On-treatment; Maintenance + Extension: on-treatment) ;
10. All grade 3-4 on-treatment non-injection site reaction related AEs by overall frequency (Maintenance: On-treatment; Extension: On-treatment; Maintenance + Extension: on-treatment);
11. Serious AEs (SAEs) by overall frequency (Induction + Maintenance: Post-baseline; Induction: Post-baseline; Maintenance: On-treatment; Extension: On-treatment; Maintenance + Extension: on-treatment) ;
12. Drug-related SAEs by overall frequency(Induction + Maintenance: Post-baseline; Extension: On-treatment; Maintenance + Extension: on-treatment);
13. AEs leading to withdrawal/permanent discontinuation of investigational product (Induction + Maintenance; Induction; Maintenance; Extension: On-treatment; Maintenance + Extension: on-treatment);
14. Summary of Injection Site Reaction Adverse Events (Event-Level Summary)
    - Percentages based on total number of ISR events within each treatment group);
    - Includes distribution of grade, duration, and event characteristics;
    - Events will be summarized according to the study medication associated with each ISR: GSK744, TMC278, GSK744 and/or TMC278.
15. Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events (Overall and by Common ISRs);
    - Percentages based on number of subjects within each treatment group;
    - Includes distribution of grade and max grade, event characteristics, number of events per subject, rate of number of events per injection visit;
    - Events will be summarized according to the study medication associated with each ISR: GSK744, TMC278, GSK744 and/or TMC278
16. Summary of Injection Site Reaction Adverse Events by Visit and Maximum Severity (Overall and by Common ISRs);

- Events will be summarized according to the study medication associated with each ISR: GSK744, TMC278, GSK744 and/or TMC278
- ISRs will be assigned based on onset date to the most recent planned IM injection visit prior or equal to the AE onset date.
- A corresponding plot of all grades and a separate plot of grade 3-4 events will be produced

17. Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events by Needle Length (Overall and by Common ISRs);
    - Needle Length will default to <=1.5 inch, unless subject has at least one administration with Needle Length >1.5 inch.
18. Summary of Total Number of Injection Site Reaction Symptoms by Visit
    - ISRs will be assigned based on onset date to the most recent planned IM injection visit prior or equal to the AE onset date.

For AEs reported more than once by a subject, the most severe intensity will be included in summaries where applicable.

If more than 10% of subjects who received IM injection enter the long-term follow-up period, the following summaries of long-term follow-up period events will be provided for the Long-Term Follow-up Period Safety Population:

1. All AEs by overall Frequency
2. All Drug-Related AEs by Overall Frequency
3. SAEs by overall Frequency.

Plots of incidence rates and relative risk for common AEs will be presented comparing each IM regimen and also for IM arms combined compared to Oral arm for the maintenance period. Onset, Duration, resolution and Severity of Headache AE, Nausea, Diarrhoea will be plotted; a similar plot will be produced for ISR events (overall and by common ISRs), with stratification according to the study medication associated with each ISR (GSK744, TMC278, GSK744 and/or TMC278) and maximum grade.

The following listings of will be provided:

1. All AEs;
2. Fatal AEs;
3. Non-fatal SAEs;
4. AEs leading to permanent discontinuation of investigational product and/or withdrawal from the study;

Additionally, a listing of subject numbers for the individual adverse events will be presented for all Post-baseline AEs.

A listing of AEs potentially related to torsades de pointes (e.g., torsades de pointes, sudden death, cardiac death, ventricular tachycardia, ventricular fibrillation and flutter,

syncope, seizures, QT or QTc prolonged) will be provided; an accompanying listing of ECG results for subjects with such AEs will also be produced.

12.3. Injection Site Reactions

Injection site reactions will be managed through AE reporting and patient diary collection throughout the study. Injection site reactions reported as AE will be summarized as part of AE data. Data collected from the patient diary will be reported separately.

In addition to AE summaries by patient, Injection site reactions reported as AE will be summarized by event, the frequency, severity, duration, resolution and intervention of injection site reaction AE by event will be provided.

A listing of grade 2 or higher injection site reaction AE will be provided.

12.4. Deaths and Serious Adverse Events

Displays for deaths and SAEs that were reported during the study will be presented as detailed in Section 17.1.3. A listing of reasons for considering an AE as serious will be produced.

12.5. Adverse Events Leading to Discontinuation of Investigational Product and/or Withdrawal from the Study and Other Significant Adverse Events

Adverse events leading to discontinuation of investigational product and/or withdrawal from the study and AEs of special interest will be reported as detailed in the Section 12.2.

12.5.1. Cardiovascular Events

Patient profile listing of subjects who experienced the cardiovascular events during the study will be provided. The cardiovascular events are listed below:

- Myocardial infarction/unstable angina
- Congestive heart failure
- Arrhythmias
- Valvulopathy
- Pulmonary hypertension
- Cerebrovascular events/stroke and transient ischemic attack
- Peripheral arterial thromboembolism
- Deep venous thrombosis/pulmonary embolism
- Revascularisation

12.5.2. Possible Suicidality-Related Adverse Event (PSRAE)

A listing of the event and description of the event will be produced for all PSRAEs reported in the study.

12.5.3. Columbia Suicide Severity Rating Scale (eCSSRS)

Positive finding data from the eCSSRS will be listed.

12.6. Pregnancies (as applicable)

A listing of any subjects becoming pregnant during the study will be provided. The outcomes of any pregnancies will be described in the CSR, where available.

12.7. Clinical Laboratory Evaluations

The following laboratory evaluations will be collected at regular intervals throughout the trial:

- Clinical chemistry (*italic text denotes parameters of special interest*):
  - fasted lipids: triglycerides, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL);
  - liver chemistries: *alanine aminotransferase (ALT)*, *aspartate aminotransferase (AST), total bilirubin(BILT)*, alkaline phosphatase (ALP);
  - electrolytes: sodium, potassium, bicarbonate, chloride;
  - renal chemistries: blood urea nitrogen (BUN), creatinine, creatinine clearance,;
  - other: *creatine kinase (creatine phosphokinase [CPK])*, *lipase*, glucose (fasted), albumin,.
- Hematology:
  - hemoglobin, hematocrit, red blood cell (RBC) count, white blood cell (WBC) count, platelet count;
  - RBC indices: mean corpuscle volume (MCV);
  - WBC differential (count and %): *neutrophils*, lymphocytes, monocytes, eosinophils, basophils;
  - coagulation tests: prothrombin time (PT), international normalized ratio (INR), partial thromboplastin time (PTT).
- Urinalysis:
  - dipstick tests: bilirubin, blood, glucose, ketones, nitrite, pH, protein, specific gravity, WBC;
  - microscopy (when potential abnormalities detected from dipstick): bacteria, RBC, RBC casts, WBC, WBC clumps, WBC casts;

- other: urine albumin/creatinine ratio.

Data not provided in the GSK standard measurement units by the central laboratory will be converted by Clinical Data Management (CDM) where necessary. Values for quantitative parameters provided as non-numeric, censored results from the central laboratory (e.g., '>100', '<1.9') will not be used when calculating summary statistics, but such values will be flagged (relative to normal ranges) and used where appropriate.

12.7.1. Listings

Listings of laboratory data for subject with grade 3/4 post-baseline emergent or grade 3/4 maintenance period treatment emergent toxicities will be presented by site, subject number, and visit. These listings will contain normal range flags, fasting flags, and toxicity grades.

12.7.2. Summaries

12.7.2.1. Summary Statistics

Summary statistics for changes from baseline at each visit will be presented by treatment group. Separate summaries will be produced for chemistry parameters of special interest, other chemistry parameters, hematology parameters, and urine concentrations. A further summary will be produced for lipids and glucose using mg/dL instead of GSK standard units.

12.7.2.2. Toxicities

A toxicity is considered post-baseline emergent in the induction period, and combined induction and maintenance period, if it develops or increases in intensity from baseline for the induction period (last available recorded toxicity up to and including the date of first induction period IP). A toxicity is considered treatment emergent relative to induction baseline if it develops or increases in intensity from the last available recorded toxicity up to and including the date of first induction period IP (typically this would be the Week -20 assessment).

A toxicity is considered treatment emergent relative to maintenance baseline if it develops or increases in intensity from the last available recorded toxicity up to and including the date of first maintenance period IP (typically this would be the Day 1 assessment).A toxicity is considered treatment emergent in the Extension Period if it occurs on-treatment during the Extension Period and develops or increases in intensity from the Extension Period baseline (last available recorded toxicity up to and including the date of first Extension Period IP exposure).Induction period specific tables will summarize the maximum post-baseline emergent grade based solely on assessments collected during the induction period. Maintenance period specific tables will summarize the maximum treatment emergent toxicity grade based on assessments collected during the maintenance period as well as long-term follow-up period assessments collected during the timeframe defined in Table 19. Overall tables for the combined Induction + Maintenance period will summarize the maximum post-baseline emergent toxicity grade

based on assessments collected during the induction and maintenance periods combined, as well as long-term follow-up period assessments collected during the timeframe defined in Table 19. For the W128 and W160 analysis, Extension Period specific tables will summarize the maximum treatment emergent toxicity grade based on assessments collected during the Extension period. For the W160 analysis, Maintenance + Extension Period specific tables will summarize the maximum treatment emergent toxicity grade based on assessments collected during the maintenance and the extension period.The number and percentage of subjects with maximum toxicities (post-baseline emergent for induction,induction plus maintenance period, and extension period tables; treatment emergent for maintenance and extension period tables) for each grade (grade 1, grade 2, etc.) and grade range (grade 1 to 4, grade 2 to 4, etc.) will be summarized by parameter and treatment group. Separate summaries will be produced for chemistry parameters and hematology parameters.

A shift table for chemistry parameters of special interest will be produced, showing baseline toxicity versus maximum treatment emergent toxicity for the maintenance period. The following will be considered parameters of special interest, but the list may change as the study progresses and data is reviewed; AST, ALT, BILT and total absolute neutrophils.

A summary and listing 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 listing of all liver chemistry data for subjects meeting hepatobiliary laboratory abnormality criteria at any post-Baseline emergent visit will also be produced.

A listing of each subject's maximum ALT and maximum bilirubin will also be produced.

12.7.2.3. Qualitative Urinalysis Results

Maximum Post-baseline emergent urine dipstick test abnormalities will be summarized.

12.7.3. Figures

Box plots of maintenance period changes from baseline, by visit, will be produced for parameters of special interest (AST, ALT, BILT and total absolute neutrophils) and other parameters which may be identified during blinded reviews.

Scatter-plots of maximum maintenance period on-treatment value versus baseline value will be presented for ALT.

Scatter-plots of maximum maintenance period on-treatment value for ALT versus maximum maintenance period on-treatment value for total bilirubin will be presented. A matrix plot of maximum maintenance period on-treatment liver chemistries and a box plot of maximum maintenance period on-treatment liver chemistries by treatment group will be produced.

The above plots will be reproduced for the Extension Switch Population on-treatment during the Extension Period at Week 128, W160, and for the randomized Q8W/Q4W IM subjects during the Maintenance + Extension Period at W160.

By study day liver chemistry (ALT, AST, and BILT) profile plots will be produced for subjects with elevations (ALT or AST ≥3xULN or ALP or BILT > 1.5xULN) at any post-baseline visit. This plot will be repeated for the Extension Switch Population with elevations at any Extension Period Visit (Extension Period data only), and for the randomized Q8W/Q4W IM subjects during the Maintenance + Extension Period

Kaplan-Meier plot of time to first treatment-emergent grade 1 or greater elevation in ALT and time to maximum treatment-emergent elevation in ALT will be provided for the maintenance period.

Other figures (such as line plots, box plots, etc.) of observed or change from baseline values over time may be produced, as needed.

12.8. Other Safety Measures

12.8.1. 12-Lead ECG

ECG findings will be listed. ECG values will be listed for each subject and change from baseline will be summarised by visit and by treatment group. Max post-baseline corrected QT intervals will also be summarized by category of value (≤450, >450 to ≤480, >480 to ≤500, and >500 msec) and max change from baseline (increase ≤30, >30 to ≤60, and >60 msec); A separate listing of ECG values for subjects with values of potential clinical concern (i.e., QTc above 480 msec or change from baseline above 60 msec) will be provided.

A listing of ECG results for subjects with AEs potentially related to torsades de pointes will be produced.

12.8.2. Vital Signs

Vital signs data will be listed for each subject. Summary statistics for change from baseline in vital signs will be presented by visit and treatment group.

12.8.3. Abacavir Hypersensitivity Reaction (HSR)

For patients experiencing an ABC HSR, data recorded on the ABC HSR eCRFs will be listed.

12.8.4. Liver Events

For subjects with liver chemistry results reaching or exceeding protocol-defined IP stopping criteria, the following data will be listed:

- liver event results exceeding the stopping criteria, and the time of the event relative to the start of study treatment and to the most recent study treatment;
- information on liver events that is used in the calculation of the Roussel Uclaf Causality Assessment Method (RUCAM) score;
- liver biopsy results;
- liver imaging results;
- past and current liver disease medical conditions;
- serology results from liver event follow-up (e.g., HCV RNA, hepatitis A IgM, CMV IgM antibody, etc.).

13. HEALTH OUTCOMES ANALYSES

Three specific questionnaires used in the study to measure patient views of their treatment are Injection site reaction diary card, HIV Treatment Satisfaction Questionnaire – HIV TSQ and HIV Medication Questionnaire-HIV MQ. Summaries of health outcomes will be performed using the OC dataset.

13.1. Humanistic Measures

13.1.1. Injection Site Reaction and Subject Activity

The number and proportion of subjects with each response (0-3) for Pain, Itching, and other symptoms as reported in the diary card will be summarised by treatment group, visit and day. Number and proportion of subjects needed home treatment or medical intervention as recorded in the diary card will be summarised by treatment group, visit and day.

Mean and median injection area symptom score from the Daily diary card will be plotted.

The number and proportion of subjects who perform cardiovascular activity, strength training and other strenuous activity will be summarized overall and by each activity.

Total weekly duration for cardiovascular activity, strength training and other strenuous activity will be summarized by treatment and visit.

13.1.2. The HIV Treatment Satisfaction Questionnaire (HIVTSQ)

The HIV Treatment Satisfaction Questionnaire (HIVTSQ) [Woodcock, 2001] and [Woodcock, 2006] was developed to evaluate treatments for HIV and patient satisfaction. The higher the score, the greater the improvement in treatment satisfaction as compared to the past few weeks. A smaller score represents a decline in treatment satisfaction compared to the past few weeks. The HIVTSQ items are summed up to produce a treatment satisfaction score (0 to 72), excluding items 7b and 9b, and an individual satisfaction rating for each item (0 to 6).

This study will be using the HIVTSQ(s) (status version) and the revised HIVTSQ(c) (change version). These measures will assess change in treatment satisfaction over time (in the same subjects) and compare current satisfaction with previous treatment satisfaction, from an earlier time point.

The number and proportion of subjects with each response (0-6) to each of the 14 items in the HIVTSQ(s) and HIVTSQ(c) will be summarised by visit and treatment group. Total satisfaction scores will be summarised by visit and treatment group using the mean, SD, median, min and max. Bar charts will be produced showing mean total satisfaction scores by treatment group and visit.

The HIVTSQs updated total scores and individual items scores for each IM arm compared to the oral arm will be tested using the Wilcoxon rank sum test at Week 32, Week 48 and Week 96, without adjustment for multiple testing. Additional scale scores (e.g. updated total scale and subscales) may be derived, pending psychometric assessment of the HIVTSQ using LATTE-2 data and guidance from the questionnaire authors on which items to include in the total scale or any subscales.

Table 30 HIVTSQ Scoring

HIVTSQs
Total Treatment Satisfaction Score
• Items 1 to 12 are summed to produce a score with a possible range of 0 to 72. • Higher scores represent greater treatment satisfaction as compared to the past few weeks. • A maximum of 6 items of these 12 items can be missing, which can be imputed to reflect the mean of the completed item scores. If 7 or more items are missing, then the overall treatment satisfaction scale score should not be computed and will remain missing. • Note: Items 7b and 9b will not be included in the derivation of the total score
Updated Total Treatment Satisfaction Score
• Items Q1–Q6; Q7a; Q8; Q9a; Q10; Q11 (range: 0-66) will be summed to produced an updated Total Treatment Satisfaction score based on guidance from the questionnaire author. • Higher scores represent greater treatment satisfaction as compared to the past few weeks. • A maximum of 5 items of these 11 items can be missing, which can be imputed to reflect the mean of the completed item scores. If 6 or more items are missing, then the updated treatment satisfaction score should not be computed and will remain missing.
Individual Item Scores
• Items are rated as 6 (very satisfied, convenient, flexible, etc.) to 0 (very dissatisfied, inconvenient, inflexible, etc.). • Higher scores represent greater satisfaction with each aspect of treatment

HIVTSQc
Total Treatment Satisfaction Score (change)
• Items 1 to 12 (excluding Items 7b and 9b) are summed to produce a score with a possible range of -33 to +33. • The higher the score, the greater the improvement in satisfaction with treatment; the lower the score, the greater the deterioration in satisfaction with treatment. A score of 0 represents no change. • A maximum of 5 of these 11 items can be missing, which can be imputed to reflect the mean of the completed item scores. If 6 or more items are missing, then the overall treatment satisfaction scale score should not be computed and will remain missing.
Individual Treatment Change Item Scores
• Items are rated as +3 ('much more satisfied', 'much more convenient', 'much more flexible', etc.) to -3 ('much less satisfied', 'much less convenient', 'much less flexible', etc.). • The higher the score, the greater the improvement in satisfaction with each aspect of treatment and the lower the score, the greater the deterioration in satisfaction with each aspect of treatment.

13.1.3. The HIV Medication Questionnaire (HIVMQ)

The HIV Medication Questionnaire (HIVMQ) will be used to assess subject reported medication adherence.

The number and proportion of subjects with each response to items a, b, d, e and f in the HIVTMQ will be summarised by treatment group, visit and medication. Items d (how often take medication as recommended), e (how often find it inconvenient or difficult to take mediation recommended) and f (how much pain/discomfort experienced) scores (0-6) will be summarised by treatment group, visit and medication using the mean, SD, median, min and max. Data from item c as free text entry will not be summarized but will be listed.

Bar charts will be produced showing mean score for items d, e and f by treatment group, visit and medication.

For each response to items a, b, d, e, and f, a combined CAB LA + RPV LA score will be derived as follows:

- For items a and b, if the responses for separate medications GSK744 LA and TMC278 differ and are both non-missing, then the combined response will be categorized as 'discordant response'. If the response for one or both medications is missing, the combined response for that item will be categorized as 'missing'.

- For items c, e, and f, the combined response will be derived as the mean value of the individual medication responses. If the response for one or both medications is missing, the combined response for that item will be categorized as 'missing'.

The combined CAB LA + RPV LA score will be summarized as defined above.

14. CLINICAL PHARMACOLOGY DATA ANALYSES

The GSK Division of Clinical Pharmacology Modelling and Simulation (CPMS) will be responsible for the PK analysis of GSK1265744. The Divisions of Clinical Pharmacology and Model-Based Drug Development at Janssen Research and Development will be responsible for conduct or oversight of the PK analysis for TMC278.

All PK and PK/PD displays will be based on the PK Population, except for the W128 analysis.

For the Week 128 analysis, PK data displays will be based on the Extension Switch Population, unless otherwise noted. Data displays will generally only use data from the Extension Period up to Week 128. Refer to Section 17.2.5 for specification of which displays will be generated for the Week 128 analysis.

14.1. Pharmacokinetic Analyses

14.1.1. Drug Concentration Measures

Plasma GSK1265744 and TMC278 concentration data will be listed and summarized by treatment, week, day, and planned sampling time. Standard summary statistics will be calculated (i.e., mean, standard deviation, median, minimum and maximum). The following summary statistics may also be calculated: geometric mean, coefficient of variation on geometric mean, 95% confidence interval for the geometric mean and standard deviation of logarithmically transformed data. Refer to the standard operating procedure, SOP-CPK-0001, for more information regarding the treatment of plasma concentrations below the assay's lower limit of quantification (NQ).

Individual plasma concentration-time profiles and median/mean profiles by treatment will be plotted. Each of the figures will contain one plot on the untransformed scale (i.e., a linear plot) and one plot on the log transformed scale (i.e., log-linear plot).

Additional data displays excluding samples collected outside of sampling windows (relative to the last dose) or that are potentially impacted by dosing irregularities will be provided.

Table 31 Sampling Windows for Evaluable Extension Period PK Concentrations for Extension Switch Population

Optimized Q4W		
TIMEPOINT	**EVALUABLE WINDOW**	**FOR PROGRAMMING:**
PRE-DOSE: W100 only	20-28 hours after last oral dose taken	20 Hours ≤ Days Since Last Oral Dose ≤ 28 Hours
2-HR-POST: W100 and W128	±0.5 hrs	1.5 hr ≤ Hours Since Last Injection ≤ 2.5 hr
1-WK-POST: W101 and W121	± 1 day	6d ≤ Days Since Last Injection ≤ 8d
PRE-DOSE: W104, W108 etc.	± 2 days	26d ≤ Days Since Last Injection ≤ 30d
Optimized Q8W		
TIMEPOINT	**EVALUABLE WINDOW**	**FOR PROGRAMMING:**
PRE-DOSE: W100 only	20-28 hours after last oral dose taken	20 Hours ≤ Days Since Last Oral Dose ≤ 28 Hours
2-HR-POST: W100 and W128	± 0.5 hrs	1.5 hr ≤ Hours Since Last Injection ≤2.5 hr
1-WK-POST: W101 and W121	± 1 day	6d ≤ Days Since Last Injection ≤ 8d
PRE-DOSE: Week 104	± 2 days	26d ≤ Days Since Last Injection ≤ 30d
PRE-DOSE: W112, 120, 128	± 4 days	52d ≤ Days Since Last Dose ≤ 60d

14.1.2. Deriving and Summarizing Pharmacokinetic Parameters

PK analysis of the plasma GSK1265744 and TMC278 concentration-time data will be conducted using non-compartmental methods with WinNonlin (Version 5.2 or higher). Actual sampling and dosing times as recorded in the eCRF will be used for analysis.

Additional PK parameters may be calculated. Pharmacokinetic data will be presented in graphical and/or tabular form and will be summarized descriptively. All pharmacokinetic data will be stored in the Archives, GlaxoSmithKline Pharmaceuticals, R&D.

The following GSK1265744 and TMC278 pharmacokinetic parameters will be estimated for IM treatment arms if adequate concentration-time data are available: AUC(0-τ), Cmax, tmax, and C_{trough}. Individual Average C_{trough} will be calculated. GSK1265744 pre-dose concentration will be estimated for oral arm.

- The first occurrence of the maximum observed plasma concentration (Cmax) and the pre-dose (trough) concentration (C_{trough}) will be determined directly from the raw concentration-time data.
- The time at which Cmax is observed will be determined directly from the raw concentration-time data (tmax).
- The area over the dosing interval at steady state (AUC(0-τ)) will be determined using the linear trapezoidal rule for increasing concentrations and the logarithmic trapezoidal rule for decreasing concentrations.

For each of these parameters, except tmax, the following summary statistics will be calculated for each treatment group: median, maximum, minimum, arithmetic mean, standard deviation, coefficient of variation on arithmetic mean, geometric mean, coefficient of variation on geometric mean, 95% confidence interval for the geometric mean and standard deviation of logarithmically transformed data. For tmax, median, maximum, minimum, arithmetic mean, and standard deviation will be calculated.

PK parameters will also be summarized by treatment and subgroups including:

- Patient reported cardiovascular activity, strength training and other strenuous activity. (yes, no)
- Total weekly duration for cardiovascular activity, strength training and other strenuous activity (< median duration, >=median duration)
- MSDF response (<50 c/mL) at Week 32 and Week 48
- PVDF at Week 32 and Week 48

For the Week 128 analysis, PK parameters will not be produced.

14.1.3. Statistical Analyses

14.1.3.1. Assessment of steady state

To examine steady state of IM treatment arms, statistical analysis of plasma GSK1265744 and TMC278 trough concentration levels will be performed separately for each analyte and treatment after $\log_e$-transformation of the concentrations. Pre-dose concentrations on Week 16-48 will be included in the analysis.

A mixed effects ANOVA model will be fitted with Week (continuous variable) as a fixed effect and subject as a random effect for each analyte and treatment separately. The Kenward & Roger (KR) degrees of freedom approach will be used. The coefficient for the slope of the day effect on the $\log_e$-scale will be used to evaluate steady state for each treatment. The 90% confidence intervals for the slope for each treatment will be calculated. If it does not appear that steady-state has been demonstrated, early weeks (e.g. Week 16, 20, 24, etc...) results will be dropped and the analysis repeated.

Plots of the arithmetic mean pre-dose concentrations against Week will be produced.

For the Week 128 analysis, this steady state analysis will not be performed given the relatively small sample size in the Extension Switch population and likelihood that steady state will not be achieved within 28 weeks based on analysis of data in the Maintenance Phase of the study.

14.2. Population PK Analysis:

A population-based PK model may be constructed based on the GSK1265744 and/or TMC278 PK data and individual Bayesian PK parameter estimates may be obtained, 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 effect of age, body size (weight, height, body surface area, and body mass index), gender, ethnic origin, HIV status, and concurrent medications (such as oral and injectable contraceptives) on GSK1265744 and/or TMC278 PK may be explored. Population PK analyses will be done under separate Population-PK Reporting and Analysis Plans.

14.3. Pharmacokinetic/Pharmacodynamic Analyses

14.3.1. Exposure-Antiviral Activity Analysis

Logistic regression will be used to exam the correlation between MSDF response (<50 c/mL) at Week 32, Week 48 and Week 96 and GSK1265744 and TMC278 PK parameters. Pearson's correlations between time to virological failure (as obtained from the MSDF algorithm) and plasma GSK1265744 and TMC278 PK parameters may be presented.

14.3.2. Exposure-Immunology Analysis

Pearson's correlations between CD4+ change from baseline and plasma GSK1265744 and TMC278 PK parameters will be summarized by treatment.

14.3.3. Exposure-Toxicity Analysis

Relationships between PK parameters and safety parameters may be explored, if needed.

Pearson's correlations between PK parameters and safety parameters (occurrence of AEs, maximum intensity of AE per subject, and clinical laboratory parameters of special

interest) may be presented. Logistic regression may be used to examine correlation between PK parameters and presence or absence of AEs of special interest from selected system organ class.

Additional factors that may be evaluated in the PK/PD analyses as covariates include age, weight, gender, race, baseline viral load, HIV risk factors, CDC classification, CD4+ cell count, CD4+ T cell activation level, cardiovascular activity, strength training, other strenuous activity, and needle length.

15. VIRAL GENOTYPING/PHENOTYPING

15.1. Genotype

For each drug class of mutations described in Section 8.6, the prevalence of On-treatment mutations will be summarized for the PDVF Genotypic population of subjects with results for the applicable DNA region (i.e., integrase or PR/RT). A similar summary will be produced for treatment emergent mutations. For the W128 analysis, only the PDVF Genotypic Extension Switch population will be used. For the W160 analysis, the PDVF Genotypic Maintenance Exposed population and the PDVF Genotypic Extension Switch population will be used.

15.2. Phenotype

The prevalence of On-treatment resistance to all ART will be summarized, once for resistance to each individual drug in each class, and again for resistance to numbers of drugs in each class.

Baseline and On-treatment FC in IC_{50} relative to wild type (WT) virus for GSK1265744, Rilpivirine (RPV), Elvitegravir (ELV) , Dolutegravir (DTG), and Raltegravir (RAL) will be summarized. A similar summary will be presented for changes in FC from baseline (i.e., On-treatment FC/baseline FC).

All phenotype data outputs will use the PDVF Phenotypic population. For the W128 analysis, only the PDVF Phenotypic Extension Switch population will be used. For the W160 analysis, the PDVF Phenotypic Maintenance Exposed population and the PDVF Phenotypic Extension Switch population will be used.

16. References

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Woodcock A, Bradley C. Validation of the Revised 10-item HIV Treatment Satisfaction Questionnaire Status Version and New Change Version. *Value in Health.* 2006;9:320-333.

17. ATTACHMENTS

17.1. Table of Contents for Data Display Specifications – Day 1

For table and figure numbering in the Clinical Study Report, prepend a '6.' for study population outputs, '7.' for efficacy, '8.' for safety, '4.' for PK, '5.' for PK/PD, and '9.' for viral genotyping and phenotyping. Listings are categorized as either 'ICH' or 'Other', regardless of the section they appear in below, and are numbered within these categories.

The table of contents references the GSK Integrated Data Standards Library (IDSL) or Therapeutic Area Standard (TST) shells for data displays, where applicable.

17.1.1. Study Population – Day 1

The ITT-E Population will be used, except where noted.

17.1.1.1. Tables

Num	Title	Details/Comments	IDSL/TST ID
1	Summary of Subject Accountability: Induction Period Conclusion Record		ES1
2	Summary of Demographic Characteristics		DM1
3	Summary of Race and Racial Combinations		DM5
4	Summary of Race and Racial Combinations Details		DM6
5	Summary of Hepatitis Status at Entry		
6	Summary of CDC Classification of HIV Infection at Baseline		CDC1
7	Summary of Current Medical Conditions		MH1
8	Distribution of Quantitative Plasma HIV-1 RNA and CD4+ Results at Screening and Baseline and Background Dual NRTI		

17.1.1.2. ICH Listings

Num	Title	Details/Comments	IDSL/TST ID
1	Listing of Induction Period Conclusion Record Reasons for Withdrawal		ES2
2	Listing of Demographic Characteristics		DM2
3	Listing of Race		DM9

17.1.1.3. Other Listings

Num	Title	Details/Comments	IDSL/TST ID
1	Listing of Study Populations	All Subjects Screened Population	
2	Listing of Subjects with Changes in Concomitant Antiretroviral Therapy		CA5

17.1.2. Efficacy –Day 1

The ITT-E Population will be used, except where noted.

17.1.2.1. Tables

Num	Title	Details/Comments	IDSL/TST ID
1	Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visits - Snapshot (MSDF) Analysis		
2	Summary of Study Outcomes (<50 copies/mL) at Day 1 – Snapshot (MSDF) Analysis		
3	Proportion of Subjects with Plasma HIV-1 RNA <200 copies/mL by Visit - Snapshot (MSDF) Analysis		
4	Summary of Study Outcomes (<200 copies/mL) at Day 1 – Snapshot (MSDF) Analysis		
5	Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit and Baseline Plasma HIV-1 RNA - Snapshot (MSDF) Analysis		
6	Cumulative Proportion of Subjects with Protocol Defined Virologic Failure by Visit		
7	Summary of Plasma HIV-1 RNA (log10 copies/mL) by Visit		
8	Summary of Change from Baseline in Plasma HIV-1 RNA (log10 copies/mL) by Visit		
9	Summary of CD4+ Cell Count (cells/mm^3) by Visit		
10	Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit		

17.1.2.2. Figures

Num	Title	Details/Comments	IDSL/TST ID
1	Proportion (95% CI) of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit – Snapshot Analysis		

17.1.2.3. ICH Listings

Num	Title	Details/Comments	IDSL/TST ID
4	Listing of Quantitative Plasma HIV-1 RNA Data		
5	Listing of Study Outcome (<50 copies/mL) at Week X – Snapshot (MSDF)		
6	Listing of Study Outcome (<200 copies/mL) at Week X – Snapshot (MSDF)		

17.1.2.4. Other Listings

Num	Title	Details/Comments	IDSL/TST ID
4	Listing of CD4+ and CD8+ Cell Count Data		

17.1.3. Safety – Day 1

The Safety Population will be used, except where noted.

17.1.3.1. Tables

Num	Title	Details/Comments	IDSL/TST ID
1	Summary of Extent of Exposure to Investigational Product		
2	Summary of All Induction Period Adverse Events by Overall Frequency for Safety Population		
3	Summary of Drug-Related Induction Period Adverse Events by Overall Frequency for Safety Population		
4	Summary of Grade 3/4 Induction Period Adverse Events by Overall Frequency for Safety Population		
5	Summary of Serious Induction Period Adverse Events by Overall Frequency for Safety Population		
6	Summary of Drug-Related Serious Induction Period Adverse Events by Overall Frequency for Safety Population		
7	Summary Induction Period Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product for Safety Population		AE1
8	Summary of Chemistry Changes from Baseline by Visit for Safety Population		LB1
9	Summary of Hematology Changes from Baseline by Visit for Safety Population		LB1
10	Summary of Maximum Treatment Emergent Clinical Chemistry Toxicities for Safety Population		
11	Summary of Maximum Treatment Emergent Hematology Toxicities for Safety Population		
12	Summary of Changes in Liver Chemistry Baseline Toxicity to Maximum On-treatment Toxicity by Baseline ALT>ULN for Safety Population		
13	Summary of QTc Values by Category for Safety Population		
14	Summary of Change from Baseline QTc Values by Category for Safety Population		
15	Summary of All Possible Suicidality-Related Adverse Events for Safety Population		

17.1.3.2. Figures

Num	Title	Details/Comments	IDSL/TST ID
1	Scatter Plots of Maximum On-treatment vs. Baseline for ALT		
2	Box Plots of Maximum On-treatment Liver Chemistries		
3	Matrix Plot of Maximum On-treatment Liver Chemistries		
4	Liver Chemistry Profile Plots for Subjects with Elevation at any Post-Baseline Visit by Study Day		
5	Scatter Plot of Maximum Post-Baseline [Parameter 1] vs. Maximum Post Baseline [Parameter 2]	DILI plot for ALT v BILI only	
6	Kaplan-Meier Plot of Time to First Treatment-Emergent Grade 1 or Greater Elevation in ALT		
7	Kaplan-Meier Plot of Time to Maximum Treatment-Emergent Elevation in ALT		
8	Figure of Onset, Duration, and Severity of Headache Adverse Events		

17.1.3.3. ICH Listings

Num	Title	Details/Comments	IDSL/TST ID
7	Listing of Investigational Product Exposure Data		HIV_IP5
8	Listing of All Adverse Events	Add the days since 1st maintenance dose.	AE8
9	Listing of Fatal Adverse Events		AE8
10	Listing of Non-Fatal Serious Adverse Events		AE8
11	Listing of Adverse Events Leading to Permanent Discontinuation of Investigational Product and/or Withdrawal from the Study		AE8
12	Listing of Subject Numbers for Individual Adverse Events		AE7

17.1.3.4. Other Listings

Num	Title	Details/Comments	IDSL/TST ID
5	Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		AE2
6	Listing of Clinical Chemistry Data for Subjects with Grade 1 or higher Abnormalities		LB5
7	Listing of Hematology Data for Subjects with Grade 1 or higher Abnormalities		LB5
8	Listing of Clinical Chemistry Laboratory Data for Subjects with Grade 3 or 4 Treatment Emergent Toxicities		LB5
9	Listing of Hematology Laboratory Data for Subjects with Grade 3 or 4 Treatment Emergent Toxicities		LB5
10	Listing of Laboratory Data for Subjects with Grade 3 or 4 Treatment Emergent Toxicities		LB5
11	Listing of Urinalysis Data for Subjects with Grade 3 or 4 Treatment Emergent Toxicities		UR2a
12	Listing of Liver Event Results and Time of Event Relative to Treatment		LIVER5
13	Listing of Past and Current Liver Disease Medical Conditions		
14	Listing of Serology Results from Liver Event Follow-up		
15	Listing of Possible Suicidality-Related Adverse Event Data: Event and Description		
16	Listing of AST, ALT, Alkaline Phosphatase, and Total Bilirubin Laboratory Data for Subjects with On-Treatment ALT at Least Two Times the ULN		
17	Listing of All Liver Chemistry Data for Subjects Meeting Hepatobiliary Laboratory Abnormality Criteria at Any Post-Baseline Emergent Visit		
18	Listing of Each Subject's Maximum ALT and Maximum Bilirubin		

17.2. Table of Contents for Data Display Specifications – Week 32/48/96/128

For table and figure numbering in the Clinical Study Report, prepend a '6.' for study population outputs, '7.' for efficacy, '8.' for safety, '9.' for PK, '10.' for PK/PD, '11.' for Health outcome and '12.' for viral genotyping and phenotyping. Listings are categorized as either 'ICH' or 'Other', regardless of the section they appear in below, and are numbered within these categories.

The table of contents references the GSK Integrated Data Standards Library (IDSL) or Therapeutic Area Standard (TST) shells for data displays, where applicable

17.2.1. Study Population – Week 32/48/96/128

The ITT-ME Population will be used, except where noted.

For the Week 32, Week 48 and Week 96 displays, unless stated otherwise, data will be summarized by randomized treatment group. Data listings will display treatment sequence for subjects switching from the randomized oral regimen to one of the selected optimized IM regimens for the extension period.

The outputs are for the Week 32, Week 48 and Week 96 reports, except where noted. Outputs for the Week 128 report will be noted in the "Reports" Column. The W128 report will only summarize/list subjects switching from the oral regimen to the optimized Q8W/Q4W IM arms (See Table 7 for treatment group descriptors).

17.2.1.1. Tables

Number	Title	Details/Comments	IDSL/ TST ID	Reports
Subject Disposition				
1.	Summary of Subject Accountability: Maintenance Period Conclusion Record		ES1	
2.	Summary of Subject Accountability (Maintenance Period): Withdrawal/Permanent Discontinuation of Investigational Product by Visit		HIV_ES1	
3.	Summary of Subject Accountability: Maintenance and Extension Period Conclusion Records	Randomized Q8W/Q4W Arms only		W96
4.	Summary of Subject Accountability: Extension Period Conclusion Record (Extension Switch Population)	Optimized Q8W/Q4W Arms Only	ES1	W96/128
5.	Summary of Subject Accountability: Withdrawal/Permanent Discontinuation of Investigational Product by Visit - Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only	HIV_ES1	W96/W128
6.	Summary of Subject Disposition at Each Study Epoch	Intent-to-Treat Population	ES4	W96
7.	Summary of Reasons for Withdrawal at Each Epoch	Intent-to-Treat Population	ES5	W96
8.	Summary of Reasons for Withdrawal During the Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only	ES5	W128
9.	Summary of Number of Subjects by Country and Site ID	Intent-to-Treat Population	NS1	W32/W48/W96
10.	Summary of Number of Subjects by Country and Site ID (Extension Switch Population)	Optimized Q8W/Q4W Arms Only	NS1	W128
Protocol Deviations				
11.	Summary of Important Protocol Deviations	Intent-To-Treat Maintenance Exposed		
12.	Summary of Important Protocol Deviations During the Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only	DV1	W128

Number	Title	Details/Comments	IDSL/ TST ID	Reports
Population Analysed				
13.	Summary of Study Populations	All Subjects Screened		W32/W48/W96
14.	Summary of Exclusions from the Per Protocol Maintenance Population	Updated Display Standard	SP2	
15.	Summary of Exclusions from the Extension Switch Population	Optimized Q8W/Q4W Arms Only	SP2	W128
Demographic and Baseline Characteristics				
16.	Summary of Demographic Characteristics	Optimized Q8W/Q4W Arms Only for W128	DM1	W32/W48/W96/ W128
17.	Summary of Race and Racial Combinations	Optimized Q8W/Q4W Arms Only for W128	DM5	W32/W48/W96/ W128
18.	Summary of Race and Racial Combinations Details	Optimized Q8W/Q4W Arms Only for W128	DM6	W32/W48/W96/ W128
19.	Summary of Age Ranges	Optimized Q8W/Q4W Arms Only for W128	DM11	W96/ W128
20.	Summary of Hepatitis Status at Entry			W32/W48/W96/
21.	Summary of Cardiovascular Risk Assessments			W32/W48/W96/
22.	Summary of CDC Classification of HIV Infection at Baseline		CDC1	W32/W48/W96/
23.	Distribution of Quantitative Plasma HIV-1 RNA and CD4+ Results at Screening and Baseline and Background Dual NRTI			W32/W48/W96/
24.	Summary of HIV Risk Factors		RF1	W32/W48/W96
25.	Summary of Associations between Subject Characteristics			W48
Prior and Concomitant Medications				
26.	Summary of Current Medical Conditions	Optimized Q8W/Q4W Arms Only for W128	MH1	W32/W48/W96/ W128
27.	Summary of Past Medical Conditions		MH1	W32/W48/W96/
28.	Summary of Concomitant Medication During Treatment by Ingredient ATC Level 1 – Induction and Maintenance Period		CM1	
29.	Summary of Concomitant Medication During Treatment by Ingredient ATC Level 1 – Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only	CM1	W128
30.	Summary of Concomitant Medication by Combination Term ATC Level 1 – Induction and Maintenance Period		CM1b	

Number	Title	Details/Comments	IDSL/ TST ID	Reports
31.	Summary of Concomitant Medication by Combination Term ATC Level 1 – Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only	CM1b	W128
32.	Summary of Concomitant Medication Ingredient Combinations – Induction and Maintenance Period		CM8	
33.	Summary of Concomitant Medication Ingredient Combinations – Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only	CM8	W128
34.	Summary of Substance Use		SU1	W96
35.	Summary of Screening Status and Reasons for Screen Failures	All Screened Population	ES6	W48/W96

17.2.1.2. ICH Listings

Number	Title	Details/Comments	IDSL/TST ID	Reports
Subject Disposition				
1.	Listing of Screen Failure Subjects			W32/W48/W96
2.	Listing of Reasons for Study Withdrawal		ES2	W32/W48/W96
3.	Listing of Reasons for Study Withdrawal During the Extension Period	Optimized Q8W/Q4W Arms Only	ES2	W128
Protocol Deviations				
4.	Listing of Important Protocol Deviations		DV2	W32/W48/W96
5.	Listing of Important Protocol Deviations During the Extension Period	Optimized Q8W/Q4W Arms Only	DV2	W128
6.	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		IE3	W96
Demographic and Baseline Characteristics				
7.	Listing of Demographic Characteristics	Optimized Q8W/Q4W Arms Only for W128	DM2	W32/W48/W96/ W128
8.	Listing of Race	Optimized Q8W/Q4W Arms Only for W128	DM9	W32/W48/W96/W128

17.2.1.3. Other Listings

Number	Title	Details/Comments	IDSL/TST ID	Reports
1.	Listing of Study Populations	All Subjects Screened Population		W32/W48/W96
2.	Listing of Subject Recruitment by Country and Site Number	All Subjects Screened Population		W32/W48/W96
3.	Listing of Subject Recruitment by Country and Site Number (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
4.	Listing of Hepatitis Test Results			W32/W48/W96
5.	Listing of CDC Classification of HIV Infection at Baseline		CDC3	W32/W48/W96/
6.	Listing of HIV Risk Factors		RF2	W32/W48/W96/
7.	Listing of Investigational Product Accountability	Optimized Q8W/Q4W Arms Only for W128		W32/W48/W96/W128
8.	Listing of Concomitant Medications	Optimized Q8W/Q4W Arms Only for W128	CM2	W32/W48/W96/W128
9.	Listing of Current and Past Medical Conditions at Baseline	Optimized Q8W/Q4W Arms Only for W128	MH2	W32/W48/W96/W128
10.	Listing of Prior Antiretroviral Therapy		CA3	W32/W48/W96
11.	Listing of Extension Period Concomitant and Post-treatment Antiretroviral Therapy (Extension Switch Population)	Optimized Q8W/Q4W Arms Only for W128. Extension Period data only.	CA5	W32/W48/W96/W128
12.	Listing of Subjects with Changes in Concomitant Antiretroviral Therapy	Optimized Q8W/Q4W Arms Only for W128	CA5	W32/W48/W96/W128
13.	Listing of Randomized and Actual Strata and Treatment Assignment	Randomized Population	TA1	W32/W48/W96
14.	Listing of Cardiovascular Risk Assessment Data			W32/W48/W96
15.	Listing of Relationship Between ATC Level 1, Ingredient and Verbatim Text		CM6	W32/W48/W96/W128
16.	Listing of Relationship Between ATC Level 4, Combination, and Verbatim Text for ART		CA7	W32/W48/W96/W128
17.	Listing of Subjects Randomized but Not Treated	Randomized Population		

17.2.2. Efficacy – Week 32/48/96/128

Unless otherwise noted, the ITT-ME Population will be used for Week 32/48/96 displays, and the Extension-Switch Population will be used for Week 128 displays. The outputs are for the Week 32, Week 48 and Week 96 reports, except where noted. Outputs for the Week 128 report will be noted in the "Reports" Column.

17.2.2.1. Tables

Number	Title	Details/ Comments	IDSL/ TST ID	Reports
1.	Summary of Analysis for Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL at Week 32/48/96 - Snapshot (MSDF) Analysis			W32/W48/W96
2.	Summary of Study Outcomes (<50 copies/mL) at Week 32/48/96/128 – Snapshot (MSDF) Analysis	Optimized Q8W/Q4W Arms Only for W128		W32/W48/W96/W128
3.	Summary of Bayesian Probability at Week 32/48: Q4W/Q8W vs. Oral 744			W32/W48
4.	Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL at Week 32/48/96 - Snapshot (MSDF) Analysis for the Per-Protocol Maintenance Population	PP-ME population		
5.	Summary of Study Outcomes (<50 copies/mL) at Week 128 – Snapshot (MSDF) Analysis for the Per-Protocol Extension Switch Population	PP- ES population		W128
6.	Summary of Bayesian Probability at Week 32/48: Q8W vs. Q4W			W32/W48
7.	Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit - Snapshot (MSDF) Analysis	Up to Week 96		

Number	Title	Details/ Comments	IDSL/ TST ID	Reports
8.	Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit during the Extension Period - Snapshot (MSDF) Analysis	Optimized Q8W/Q4W Arms Only, up to Week 128		W128
9.	Proportion of Subjects with Plasma HIV-1 RNA <200 copies/mL by Visit - Snapshot (MSDF) Analysis	Up to Week 96		
10.	Proportion of Subjects with Plasma HIV-1 RNA <200 copies/mL by Visit during the Extension Period - Snapshot (MSDF) Analysis	Optimized Q8W/Q4W Arms Only, up to Week 128		W128
11.	Summary of Study Outcomes (<200 copies/mL) at Week 32/48/96/128 – Snapshot (MSDF) Analysis	Optimized Q8W/Q4W Arms Only for W128		W32/W48/W96/W128
12.	Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit and Baseline Plasma HIV-1 RNA - Snapshot (MSDF) Analysis	Up to Week 96		
13.	Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit and Derived Plasma HIV-1 RNA <50 c/mL Prior to Week -8 - Snapshot (MSDF) Analysis	Up to Week 96		
14.	Proportion of Responders at Week 32/48/96 based on Snapshot (MSDF) Analysis by Week First Suppressed			W32/W48/W96
15.	Cumulative Proportion of Subjects with Maintenance Period Protocol Defined Virologic Failure by Visit			
16.	Cumulative Proportion of Subjects with Extension Period Protocol Defined Virologic Failure by Visit (Extension Switch Population)	Optimized Q8W/Q4W Arms Only, up to Week 128		W128
17.	Summary of Kaplan-Meier Estimates of Proportion of Subjects Without Virologic or Tolerability Failure at Week 32/48/96 – Maintenance Period			

Number	Title	Details/ Comments	IDSL/ TST ID	Reports
18.	Distribution of Quantitative Plasma HIV-1 RNA Results at Suspected and Confirmation of Maintenance Period Protocol Defined Virologic Failure			
19.	Distribution of Quantitative Plasma HIV-1 RNA Results at Suspected and Confirmation of Extension Period Protocol Defined Virologic Failure	Optimized Q8W/Q4W Arms Only, up to Week 128		W128
20.	Summary of Plasma HIV-1 RNA (log10 copies/mL) by Visit			
21.	Summary of Change from Baseline in Plasma HIV-1 RNA (log10 copies/mL) by Visit			
22.	Summary of CD4+ Cell Count (cells/mm^3) by Visit			
23.	Summary of CD4+ Cell Count (cells/mm^3) by Visit - Extension Period	Optimized Q8W/Q4W Arms Only for W128		W128
24.	Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit			
25.	Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit - Extension Period	Optimized Q8W/Q4W Arms Only for W128 Note: Baseline is last value up to and including the date of first extension injection		W128
26.	Summary of CD8+ Cell Count (cells/mm^3) by Visit			
27.	Summary of Change from Baseline in CD8+ Cell Count (cells/mm^3) by Visit			

Number	Title	Details/ Comments	IDSL/ TST ID	Reports
28.	Summary of HIV-1 Associated Conditions Including Recurrences - Maintenance Period		HIV1	
29.	Summary of HIV-1 Associated Conditions Including Recurrences - Extension Period	Optimized Q8W/Q4W Arms Only	HIV1	W128
30.	Summary of HIV-1 Associated Conditions Excluding Recurrences - Maintenance Period		HIV1	
31.	Summary of HIV-1 Associated Conditions Excluding Recurrences - Extension Period	Optimized Q8W/Q4W Arms Only	HIV1	W128
32.	Summary of HIV-1 Associated Conditions Progression of HIV Disease - Maintenance Period		HIV2	
33.	Summary of HIV-1 Associated Conditions Progression of HIV Disease - Extension Period	Optimized Q8W/Q4W Arms Only	HIV2	W128
34.	Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit and [Subgroup] – Snapshot (MSDF) Analysis	See Section 8.2 for criteria on which subgroup variables to include (if any).		
35.	Summary of Study Outcomes (<50 copies/mL) at Week 32/48/96 by [Subgroup] – Snapshot (MSDF) Analysis	As above		W32/W48/W96
36.	Proportion of Subjects with Plasma HIV-1 RNA <2 copies/mL by Visit – Observed Case Analysis	Based on BIOMNTR data Up to Week 96		

Number	Title	Details/ Comments	IDSL/ TST ID	Reports
37.	Proportion of Subjects with Plasma HIV-1 RNA <2 copies/mL by Visit during Extension Period– Observed Case Analysis	Based on BIOMNTR data Optimized Q8W/Q4W Arms Only for W128		W128
38.	Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit (Observed Case Analysis) – Maintenance and Extension Period	- Randomized Q8W/Q4W Arms Only - Maintenance and Extension periods		W96
39.	Proportion of Subjects with Extension Period Plasma HIV-1 RNA <50 copies/mL by Visit (Observed Case Analysis) – Extension Switch Population	- Extension Period data for Optimized Q8W/Q4W Arms		W96/W128
40.	Cumulative Proportion of Subjects with Protocol Defined Virologic Failure by Visit – Maintenance and Extension Period	- Randomized Q8W/Q4W Arms Only - Data from Maintenance and Extension periods		W96
41.	Cumulative Proportion of Subjects in the Extension Period with Protocol Defined Virologic Failure by Visit (Extension Switch Population)	- Extension Period data for Optimized Q8W/Q4W Arms Extension periods		W96/W128

17.2.2.2. Figures

Number	Title	Details/Comments	IDSL/TST ID	Reports
1.	Proportion (95% CI) of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit – Snapshot Analysis (Induction and Maintenance Period)	Up to Week 96		
2.	Proportion (95% CI) of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit – Snapshot Analysis (Extension Period)	Optimized Q8W/Q4W Arms, up to Week 128		W128
3.	Individual Plasma HIV-1 RNA (log10 copies/mL) and CD4+ Cell Count Profiles by Visit			
4.	Kaplan-Meier Plot of Time to Virologic or Tolerability Failure – Maintenance Period			
5.	Proportion (95% CI) of Subjects with Virologic Failure by Visit – Snapshot Analysis (Induction and Maintenance Period)	Up to Week 96		
6.	Proportion (95% CI) of Subjects with Virologic Failure by Visit (Maintenance Period) – Snapshot Analysis	Day 1 to Week 96		
7.	Proportion (95% CI) of Subjects with Virologic Failure by Visit (Extension Period) – Snapshot Analysis	Optimized Q8W/Q4W Arms, up to Week 128.		W128
8.	Individual Plasma HIV-1 RNA (log10 copies/mL) Profiles by Visit – Q8W IM Subjects			
9.	Individual Plasma HIV-1 RNA (log10 copies/mL) Profiles by Visit – Q4W IM Subjects			
10.	Individual Plasma HIV-1 RNA (log10 copies/mL) Profiles by Visit – Oral 744 Subjects	Add annotation of extension period regimen (optimized Q8W or Q4W)		
11.	Individual Plasma HIV-1 RNA (log10 copies/mL) Profiles by Visit - Extension Period (Extension-Switch Subjects)	Optimized Q8W/Q4W Arms, up to Week 128.		W128

17.2.2.3. ICH Listings

Number	Title	Details/Comments	IDSL/TST ID	Reports
7.	Listing of Quantitative Plasma HIV-1 RNA Data	Extension-Switch Subjects during Extension Period Only for W128		W32/W48/W96/W128
8.	Listing of Study Outcome (<50 copies/mL) at Week 32/48/96/128 – Snapshot (MSDF)	Extension-Switch Subjects Only for W128		W32/W48/W96/W128
9.	Listing of Study Outcome (<200 copies/mL) at Week 32/48/96/128 – Snapshot (MSDF)	Extension-Switch Subjects Only for W128		W32/W48/W96/W128

17.2.2.4. Other Listings

Number	Title	Details/Comments	IDSL/TST ID	Reports
17.	Listing of CD4+ and CD8+ Cell Count Data			
18.	Listing of Extension Period CD4+ Cell Count Data	Optimized Q8W/Q4W Arms, up to Week 128		W128
19.	Listing of HIV-1 Associated Conditions		HIV4	
20.	Listing of Extension Period HIV-1 Associated Conditions	Optimized Q8W/Q4W Arms, up to Week 128		W128
21.	Listing of Background NRTI Switches			
22.	Listing of Subjects with Protocol Defined Virologic Failure			
23.	Listing of Subjects with Extension Period Protocol Defined Virologic Failure	Optimized Q8W/Q4W Arms Only		W128
24.	Listing of Quantitative Plasma HIV-1 RNA Data for Subjects Classified as Having 'data in window >50' at any Maintenance Period Visit based on the Snapshot Classification			
25.	Listing of Quantitative Plasma HIV-1 RNA Data for Extension-Switch Subjects Classified as Having 'data in window >50' at any Extension Period Visit based on the Snapshot Classification	Optimized Q8W/Q4W Arms Only		W128
26.	Listing of Quantitative Plasma HIV-1 RNA Data for Subjects with HIV-1 RNA ≥ 50 c/mL at any time during the Maintenance Period or Extension Period			W96
27.	Listing of BIOMNTR Viral Load Results			
28.	Listing of BIOMNTR Viral Load Results – Extension Period	Optimized Q8W/Q4W Arms Only		W128

17.2.3. Safety – Week 32/48/96/128

Unless otherwise noted, the Safety-ME Population will be used for Week 32/48/96 displays, and the Extension-Switch Population will be used for W128 displays. Outputs for the Week 128 report will be noted in the “Reports” Column in the following tables.

17.2.3.1. Tables

Number	Title	Details/Comments	IDSL/TST ID	Reports
1.	Summary of Extent of Exposure to Investigational Product (Induction and Maintenance Period)			
2.	Summary of Extent of Exposure to Investigational Product – Maintenance and Extension Period	Randomized Q8W/Q4W Arms Only		
3.	Summary of Extent of Exposure to Investigational Product (Extension Switch Population) – Extension Period	Optimized Q8W/Q4W Arms Only		W96/W128
Adverse Events (AEs)				
4.	Summary of All Post-baseline Adverse Events by System Organ Class – Induction and Maintenance Period		AE1	
5.	Summary of All Post-baseline Adverse Events by Overall Frequency – Induction and Maintenance Period			
6.	Summary of All Induction Period Adverse Events by Overall Frequency			
7.	Summary of All Maintenance Period On-treatment Adverse Events by Overall Frequency			
8.	Summary of All Extension Period On-treatment Adverse Events by Overall Frequency (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
9.	Summary of All Long-term Follow-up Period Adverse Events by Overall Frequency (Safety Long-Term Follow-up Population)	Provide if >10% IM subjects enter long term follow up		
10.	Summary of All Post-baseline Adverse Events by System Organ Class and Maximum Toxicity – Induction and Maintenance Period		AE5 or AE5b	
11.	Summary of All Induction Period Adverse Events by System Organ Class and Maximum Toxicity		AE5 or AE5b	
12.	Summary of All Maintenance Period On-treatment Adverse Events by System Organ Class and Maximum Toxicity		AE5 or AE5b	

Number	Title	Details/Comments	IDSL/TST ID	Reports
13.	Summary of All On-Treatment Adverse Events by System Organ Class and Maximum Toxicity – Maintenance and Extension Period	Randomized Q8W/Q4W Arms Only	AE5 or AE5b	
14.	Summary of Extension Period On-treatment Adverse Events by System Organ Class and Maximum Toxicity (Extension Switch Population)	Optimized Q8W/Q4W Arms Only	AE5 or AE5b	W96/W128
15.	Summary of Common (>=3%) Grade 2-4 Post-baseline Adverse Events by Overall Frequency – Induction and Maintenance Period			
16.	Summary of Common (>=3%) Grade 2-4 Extension Period Adverse Events by Overall Frequency (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
17.	Summary of Common (>=5%) Non-Serious Post-baseline Adverse Event by System Organ Class and Preferred Term (Number of Subjects and Occurrences) – Induction and Maintenance Period			
18.	Summary of Common (>=5%) Extension Period Non-Serious Adverse Event by System Organ Class and Preferred Term (Number of Subjects and Occurrences/Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
19.	Summary of Grade 3/4 Post-baseline Adverse Events by Overall Frequency – Induction and Maintenance Period			
20.	Summary of Grade 3/4 Maintenance Period On-treatment Adverse Events by Overall frequency			
21.	Summary of Grade 3/4 Extension Period On-treatment Adverse Events by Overall Frequency (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
22.	Summary of Grade 3/4 Maintenance Period On-treatment Non Injection Site Reaction Related Adverse Events by Overall Frequency			
23.	Summary of Grade 3/4 Extension Period On-treatment Non Injection Site Reaction Related Adverse Events by Overall Frequency (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
24.	Summary of Drug-Related Post-baseline Adverse Events by Overall Frequency – Induction and Maintenance Period			

Number	Title	Details/Comments	IDSL/TST ID	Reports
25.	Summary of Drug-Related Extension Period On-treatment Adverse Events by Overall Frequency (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
26.	Summary of All Drug-Related Post-baseline Adverse Events by System Organ Class and Preferred Term and Maximum Toxicity – Induction and Maintenance Period		AE5 or AE5b	
27.	Summary of Drug-Related Induction Period Adverse Events by System Organ Class and Maximum Toxicity		AE5 or AE5b	
28.	Summary of Drug-Related Maintenance Period On-treatment Adverse Events by System Organ Class and Maximum Toxicity		AE5 or AE5b	
29.	Summary of All Drug-Related On-treatment Adverse Events by System Organ Class and Maximum Toxicity – Maintenance and Extension Period	Randomized Q8W/Q4W Arms Only	AE5 or AE5b	
30.	Summary of Drug-Related Extension Period On-treatment Adverse Events by System Organ Class and Maximum Toxicity (Extension Switch Population)	Optimized Q8W/Q4W Arms Only	AE5 or AE5b	W96/W128
31.	Summary of Long-Term Follow-up Period Drug-Related Adverse Events by Overall Frequency (Safety Long-Term Follow-Up Population)	Provide if >10% IM subjects enter long term follow up		
32.	Summary of Common (>=3%) Drug-Related Grade 2-4 Post-baseline Adverse Events by Overall Frequency – Induction and Maintenance Period			
33.	Summary of Extension Period Common (>=3%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
Serious and Other Significant Adverse Events				
34.	Summary of Post-baseline Serious Adverse Events by Overall Frequency – Induction and Maintenance Period			
35.	Summary of Serious Induction Period Adverse Events by Overall			
36.	Summary of Serious Maintenance Period On-treatment Adverse Events by Overall Frequency			

Number	Title	Details/Comments	IDSL/TST ID	Reports
37.	Summary of Post-baseline Serious Adverse Events by Overall Frequency – Maintenance and Extension Period	Randomized Q8W/Q4W Arms Only		
38.	Summary of Serious Extension Period On-treatment Adverse Events by Overall Frequency (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W96/W128
39.	Summary of Long-Term Follow-up Period Serious Adverse Events by Overall Frequency (Safety Long-Term Follow-up Population)	Provide if >10% IM subjects enter long term follow up,		
40.	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences) – Induction and Maintenance Period	new		
41.	Summary of Extension Period Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences) -Extension Switch Population	Optimized Q8W/Q4W Arms Only		W128
42.	Summary of Post-baseline Drug-Related Serious Adverse Events by Overall Frequency – Induction and Maintenance Period			
43.	Summary of Extension Period Drug-Related Serious Adverse Events by Overall Frequency (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
44.	Summary of Maintenance Period Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class		AE1	
45.	Summary of Extension Period Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class	Randomized Q8W/Q4W Arms Only		
46.	Summary of Extension Period Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W96/W128
47.	Summary of Drug-Related Grade 3/4 Post-baseline Adverse Events by Overall Frequency – Induction and Maintenance Period			

Number	Title	Details/Comments	IDSL/TST ID	Reports
48.	Summary of Extension Period Drug-Related Grade 3/4 Adverse Events by Overall Frequency (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
49.	Summary of Grade 3/4 Maintenance Period On-treatment Non Injection Site Reaction Related Adverse Events by Overall Frequency - Drug-related			
50.	Summary of Grade 3/4 Extension Period Non Injection Site Reaction Related Adverse Events by Overall Frequency - Drug-related (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
Injection Site Reaction Adverse Events				
51.	Summary of Injection Site Reaction Adverse Events (Event-Level Summary) – Maintenance Period			
52.	Summary of Injection Site Reaction Adverse Events (Event-Level Summary) – Maintenance and Extension Period	Randomized Q8W/Q4W Arms Only		
53.	Summary of Injection Site Reaction Adverse Events (Event-Level Summary) – Extension Switch Population	Optimized Q8W/Q4W Arms Only. Summarize AEs during Extension Period only for W128		W96/W128
54.	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events – Overall and Common (Maintenance Period)			
55.	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events – Overall and Common (Maintenance and Extension Period)	Randomized Q8W/Q4W Arms Only		
56.	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events – Overall and Common (Extension Switch Population)	Optimized Q8W/Q4W Arms Only. Summarize AEs during Extension Period only for W128		W96/W128
57.	Summary of Injection Site Reaction Adverse Events by Visit and Maximum Severity – Overall and Common (Maintenance Period)			

Number	Title	Details/Comments	IDSL/TST ID	Reports
58.	Summary of Extension Period Injection Site Reaction Adverse Events by Visit and Maximum Severity – Overall and Common (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
59.	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events by Needle Length – Overall and Common (Maintenance Period)			
60.	Summary of Extension Period Subject-Level Characteristics of Injection Site Reaction Adverse Events by Needle Length – Overall and Common (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
61.	Summary of Total Number of Injection Site Reaction Adverse Events by Visit (Maintenance Period)			
62.	Summary of Extension Period Total Number of Injection Site Reaction Adverse Events by Visit (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
63.	Summary of Injection Site Reaction Adverse Events (Event-Level Summary) - GSK1265744			
64.	Summary of Extension Period Injection Site Reaction Adverse Events (Event-Level Summary) - GSK1265744 (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
65.	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events - Overall and Common (GSK1265744)			
66.	Summary of Subject-Level Characteristics of Extension Period Injection Site Reaction Adverse Events - Overall and Common - GSK1265744 (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
67.	Summary of Overall and Common Injection Site Reaction Adverse Events by Visit and Maximum Severity - GSK1265744			
68.	Summary of Overall and Common Extension Period Injection Site Reaction Adverse Events by Visit and Maximum Severity - GSK1265744 (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
69.	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events by Needle Length - Overall and Common (GSK1265744)			

Number	Title	Details/Comments	IDSL/TST ID	Reports
70.	Summary of Total Number of Injection Site Reaction Adverse Events by Visit - GSK1265744			
71.	Summary of Total Number of Extension Period Injection Site Reaction Adverse Events by Visit - GSK1265744 (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
72.	Summary of Injection Site Reaction Adverse Events (Event-Level Summary) - TMC278			
73.	Summary of Extension Period Injection Site Reaction Adverse Events (Event-Level Summary) - TMC278(Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
74.	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events - Overall and Common (TMC278)			
75.	Summary of Subject-Level Characteristics of Extension Period Injection Site Reaction Adverse Events - Overall and Common - TMC278 (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
76.	Summary of Overall and Common Injection Site Reaction Adverse Events by Visit and Maximum Severity -TMC278			
77.	Summary of Overall and Common Extension Period Injection Site Reaction Adverse Events by Visit and Maximum Severity -TMC278 (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
78.	Summary of Subject-Level Characteristics of Injection Site Reaction Adverse Events by Needle Length - Overall and Common (TMC278)			
79.	Summary of Total Number of Injection Site Reaction Adverse Events by Visit - TMC278			
80.	Summary of Total Number of Extension Period Injection Site Reaction Adverse Events by Visit - TMC278 (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128

Number	Title	Details/Comments	IDSL/TST ID	Reports
Laboratory: Chemistry and Hematology				
81.	Summary of Chemistry Changes from Baseline by Visit – Induction and Maintenance Period	Includes lipids and Glucose in Conventional Units	LB1	
82.	Summary of Chemistry Changes from Baseline by Visit – Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only Note: Baseline is last value up to and including the date of first extension injection		W128
83.	Summary of Hematology Changes from Baseline by Visit – Induction and Maintenance		LB1	
84.	Summary of Hematology Changes from Baseline by Visit – Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only Note: Baseline is last value up to and including the date of first extension injection		W128
85.	Summary of Maximum Post-baseline Emergent Clinical Chemistry Toxicities – Induction and Maintenance Period			
86.	Summary of Maximum Maintenance Period Treatment Emergent Clinical Chemistry Toxicities – Induction and Maintenance Period			
87.	Summary of Maximum Extension Period Treatment Emergent Clinical Chemistry Toxicities (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
88.	Summary of Maximum Post-baseline Emergent Hematology Toxicities – Induction and Maintenance Period			
89.	Summary of Maximum Maintenance Period Treatment Emergent Hematology Toxicities – Induction and Maintenance Period			
90.	Summary of Maximum Extension Period Treatment Emergent Hematology Toxicities (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128

Number	Title	Details/Comments	IDSL/TST ID	Reports
91.	Summary of Changes in Clinical Chemistry Baseline Toxicity to Maximum Maintenance Period On-Treatment Toxicity - Parameters of Special Interest	Parameters of Special Interest: AST, ALT, ALP,Total Bilirubin Note: Baseline is last value up to and including the date of first extension injection		
92.	Summary of Changes in Clinical Chemistry Baseline Toxicity to Maximum Extension Period On-Treatment Toxicity - Parameters of Special Interest (Extension Switch Population)	Parameters of Special Interest: AST, ALT, ALP,Total Bilirubin Note: Baseline is last value up to and including the date of first extension injection		W128
Laboratory: Urinalysis				
93.	Summary of Post-Baseline Emergent Urinalysis Dipstick Results – Induction and Maintenance Period		UR3/LB2	
94.	Summary of Urine Concentration Changes from Baseline by Visit – Induction and Maintenance Period	Includes Baseline values.	LB1	
95.	Summary of Urine Concentration Changes from Baseline by Visit – Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only Note: Baseline is last value up to and including the date of first extension injection.	LB1	W128

Number	Title	Details/Comments	IDSL/TST ID	Reports
Laboratory: Hepatobiliary (Liver)				
96.	Listing of Liver Monitoring/Stopping Event Reporting (Updated Display Standard)	Updated Display Standard	LIVER5	
97.	Listing of Liver Monitoring/Stopping Event Reporting During the Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only Updated Display Standard	LIVER5	W128
98.	Summary of Subjects Meeting Hepatobiliary Laboratory Abnormality Criteria (Post-Baseline Emergent) – Induction and Maintenance Period			
99.	Listing of Subjects Meeting Hepatobiliary Laboratory Abnormality Criteria at Any Post-Baseline Emergent Visit			
100.	Summary of Hepatobiliary Laboratory Abnormalities (Updated Display Standard) – Induction and Maintenance Period	Updated Display Standard	LIVER10	
101.	Summary of Hepatobiliary Laboratory Abnormalities (Updated Display Standard) – Maintenance and Extension Period	Updated Display Standard Randomized Q8W/Q4W Arms Only	LIVER10	W96
102.	Summary of Extension Period Hepatobiliary Laboratory Abnormalities (Updated Display Standard) – Extension Switch Population	Updated Display Standard Optimized Q8W/Q4W Arms Only	LIVER10	W96/W128
103.	Listing of Subjects Meeting Hepatobiliary Laboratory Criteria Post-Baseline (Updated Display Standard)	Updated Display Standard	LIVER13	W96
104.	Listing of Subjects Meeting Hepatobiliary Laboratory Criteria during the Extension Period – Updated Display Standard (Extension Switch Population)	Optimized Q8W/Q4W Arms Only	LIVER13	W128

Number	Title	Details/Comments	IDSL/TST ID	Reports
ECG				
105.	Summary of Change from Baseline in ECG Values by Visit – Induction and Maintenance Period		EG2	
106.	Summary of Change from Baseline in ECG Values by Visit – Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only Note: Note: Baseline is last value before the date of first extension injection.	EG2	W128
107.	Summary of QTc Values by Category – Induction and Maintenance Period			
108.	Summary of QTc Values by Category – Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only		W128
109.	Summary of Change from Baseline QTc Values by Category – Induction and Maintenance Period			
110.	Summary of Change from Baseline QTc Values by Category – Extension Period (Extension Switch Population)	Optimized Q8W/Q4W Arms Only Note: Note: Baseline is last value before the date of first extension injection.		W128
Vital Signs				
111.	Summary of Change From Baseline in Vital Signs by Visit – Induction and Maintenance Period	Include BMI	VS1	
112.	Summary of Change from Baseline in Vital Signs by Visit – Extension Period (Extension Switch Population)		VS1	W128
113.	Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1 - Section 2)		PSRAE1	
114.	Listing of Possible Suicidality-Related Adverse Event Data: Possible Cause(s) (Section 3)		PSRAE3	

Number	Title	Details/Comments	IDSL/TST ID	Reports
115.	Listing of Possible Suicidality-Related Adverse Event Data (Section 4)		PSRAE4	
116.	Listing of Possible Suicidality-Related Adverse Event Data (Section 5 - Section 8)		PSRAE5	
117.	Listing of eCSSRS Suicidal Ideation and Behaviour Data For Subjects With at least One Positive Response for Suicidal Indication Alert			
118.	Listing of eCSSRS Suicidal Behaviour Details For Subjects With at least One Positive Response for Suicidal Indication Alert			
119.	Listing of eCSSRS Details of Most Severe Suicidal Ideation For Subjects With at least One Positive Response for Suicidal Indication Alert			

17.2.3.2. Figures

Number	Title	Details/Comments	IDSL/TST ID	Reports
1.	Plot of Common Maintenance Period On-treatment Adverse Events and Relative Risk– Q8W vs. Oral		AE10	
2.	Plot of Common Maintenance Period On-treatment Adverse Events and Relative Risk– Q4W vs. Oral		AE10	
3.	Plot of Common Maintenance Period On-treatment Adverse Events and Relative Risk– Q8W vs. Q4W		AE10	
4.	Plot of Common Maintenance Period On-treatment Adverse Events and Relative Risk– IM Subtotal vs. Oral		AE10	
5.	Box Plots of Maintenance Period Change from Baseline of Aspartate Amino Transferase (AST) ((IU/L) over Time	Repeat for other Parameters of Special Interest: ALT, ALP, Total Bilirubin, total absolute neutrophils.		
6.	Scatter Plots of Maximum Maintenance Period On-Treatment vs. Baseline for ALT			
7.	Scatter Plots of Maximum Extension Period On-Treatment vs. Baseline for ALT (Extension Switch Population)	Note: Baseline is last value up to and including date of first extension injection.		W128
8.	Box Plots of Maximum Maintenance Period On-treatment Liver Chemistries			
9.	Matrix Plot of Maximum Maintenance Period On-treatment Liver Chemistries			
10.	Matrix Plot of Maximum Extension Period On-treatment Liver Chemistries (Extension Switch Population)			W128
11.	Liver Chemistry Profile Plots for Subjects with Elevation at any Post-Baseline Visit by Study Day			
12.	Liver Chemistry Profile Plots for Subjects with Elevation during the Extension Period by Study Day (Extension Switch Population)	Extension Period Only		W128
13.	Scatter Plot of Maximum Maintenance Period On-Treatment Value: [Parameter 1] vs. [Parameter 2]	DILI plot for ALT v BILI only		
14.	Scatter Plot of Maximum Extension Period On-Treatment Value: [Parameter 1] vs. [Parameter 2] (Extension Switch Population)	DILI plot for ALT v BILI only		W128

Number	Title	Details/Comments	IDSL/TST ID	Reports
15.	Kaplan-Meier Plot of Time to First Maintenance Period Treatment-Emergent Grade 1 or Greater Elevation in ALT			
16.	Kaplan-Meier Plot of Time to Maximum Maintenance Period Treatment-Emergent Elevation in ALT			
17.	Figure of Onset, Duration, and Severity of Headache Adverse Events – Induction and Maintenance Period			
18.	Plot of Common Maintenance Period Injection Site Adverse Events and Relative Risk: Q8W vs. Q4W			
19.	Figure of Onset, Duration, and Severity of Overall and Common Maintenance Period Injection Site Reaction Adverse Events by Maximum Grade: GSK744 LA or TMC278 LA	Repeat parameters for "GSK126574', 'TMC278'		
20.	Figure of Onset, Duration, and Severity of Overall and Common Extension Period Injection Site Reaction Adverse Events by Maximum Grade: GSK744 LA or TMC278 LA (Extension Switch Population)			W128
21.	Figure of Incidence of Maintenance Period Injection Site Reaction Adverse Events – Overall and Common —GSK 744 LA or TMC278 LA	Repeat parameters for "GSK126574', 'TMC278'		
22.	Figure of Incidence of Extension Period Injection Site Reaction Adverse Events – Overall and Common —GSK 744 LA or TMC278 LA (Extension Switch Population)			W128
23.	Figure of Incidence of Grade 3-4 Maintenance Period Injection Site Reaction Adverse Events – Overall and Common—GSK 744 LA or TMC278 LA	Repeat parameters for "GSK126574', 'TMC278'		
24.	Figure of Incidence of Grade 3-4 Extension Period Injection Site Reaction Adverse Events – Overall and Common—GSK 744 LA or TMC278 LA (Extension Switch Population)			W128

17.2.3.3. ICH Listings

Number	Title	Details/Comments	IDSL/ TST ID	Report
10.	Listing of Investigational Product Exposure Data		HIV_IP5	
11.	Listing of Investigational Product Exposure Data during the Extension Period (Extension Switch Population)			W128
12.	Listing of All Adverse Events	Add the days since 1st maintenance dose.	AE8	
13.	Listing of All Extension Period Adverse Events (Extension Switch Population)			W128
14.	Listing of Fatal Adverse Events		AE8	
15.	Listing of Extension Period Fatal Adverse Events (Extension Switch Population)			W128
16.	Listing of Non-Fatal Serious Adverse Events		AE8	
17.	Listing of Extension Period Non-Fatal Serious Adverse Events (Extension Switch Population)			W128
18.	Listing of Reasons for Considering an AE as Serious	Moved from Other Listings	AE14	W32/W48/W96/W128
19.	Listing of Adverse Events Leading to Permanent Discontinuation of Investigational Product and/or Withdrawal from the Study		AE8	
20.	Listing of Extension Period Adverse Events Leading to Permanent Discontinuation of Investigational Product and/or Withdrawal from the Study (Extension Switch Population)			W128
21.	Listing of Subject Numbers for Individual Adverse Events		AE7	
22.	Listing of Subject Numbers for Individual Extension Period Adverse Events (Extension Switch Population)			W128
23.	Listing of Subjects Who Became Pregnant During the Study		PREG1a	
24.	Listing of Extension Switch Subjects Who Became Pregnant during the Extension Period			W128
25.	Listing of ECG Values		EG3	
26.	Listing of Extension Period ECG Values (Extension Switch Population)			W128

Number	Title	Details/Comments	IDSL/ TST ID	Report
27.	Listing of ECG Values for Subjects with a Value of Potential Clinical Concern		EG3	
28.	Listing of ECG Values for Subjects with a Value of Potential Clinical Concern during the Extension Period (Extension Switch Population)			W128
29.	Listing of ECG Findings		EG5	
30.	Listing of Extension Period ECG Findings (Extension Switch Population)			W128
31.	Listings of Vital Signs		VS4	
32.	Listings of Extension Period Vital Signs (Extension Switch Population)	Including baseline findings		W128
Laboratory: Hepatobiliary (Liver)				
33.	Listing of Medical Conditions for Subjects with Liver Stopping Events		MH2	W96
34.	Listing of Medical Conditions for Subjects with Liver Stopping Events during the Extension Period (Extension Switch Population)			W128
35.	Listing of Substance Use for Subjects with Liver Stopping Events		SU2	W96
36.	Listing of Substance Use for Subjects with Liver Stopping Events during the Extension Period (Extension Switch Population)			W128

17.2.3.4. Other Listings

Number	Title	Details/ Comments	IDSL/TST ID	Report
29.	Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		AE2	W32/W48/W96/ W128
30.	Listing of Clinical Chemistry Laboratory Data for Subjects with Grade 3/4 Post Baseline Emergent or Grade 3/4 Maintenance Period Treatment-Emergent Toxicities		LB5	
31.	Listing of Extension Period Clinical Chemistry Laboratory Data for Subjects with Grade 3/4 Extension Period Treatment-Emergent Toxicities (Extension Switch Population)			W128
32.	Listing of Hematology Laboratory Data for Subjects with Grade 3/4 Post Baseline Emergent or Grade 3/4 Maintenance Period Treatment-Emergent Toxicities		LB5	
33.	Listing of Extension Period Hematology Laboratory Data for Subjects with Grade 3/4 Extension Period Treatment-Emergent Toxicities (Extension Switch Population)			W128

Number	Title	Details/ Comments	IDSL/TST ID	Report
34.	Listing of Urinalysis Data for Subjects with Grade 3/4 Post Baseline Emergent or Grade 3/4 Maintenance Period Treatment-Emergent Toxicities		UR2a	
35.	Listing of Extension Period Urinalysis Data for Subjects with Grade 3/4 Extension Period Treatment-Emergent Toxicities (Extension Switch Population)			W128
36.	Listing of Abacavir Hypersensitivity Reaction Record - Exposure to Abacavir		ABC_HSR_EXPO2	
37.	Listing of Abacavir Hypersensitivity Reaction Record - Subject History of Drug Allergies		ABC_HSR_DRUG2	
38.	Listing of Abacavir Hypersensitivity Reaction Record - Subject and Family Conditions		ABC_HSR COND2	
39.	Listing of Abacavir Hypersensitivity Reaction Record - Skin Rash Details		ABC_HSR_RASH2	
40.	Listing of Abacavir Hypersensitivity Reaction Record - Symptoms		ABC_HSR_SYMP4	
41.	Listing of Abacavir Hypersensitivity Reaction Record - Vital Signs		VS4	
42.	Listing of Abacavir Hypersensitivity Reaction Record - Individual Symptoms and Diagnostic Category Assignments (Excluding Other Symptoms)		ABC_HSR_SYMP6	
43.	Listing of Abacavir Hypersensitivity Reaction Record - Individual Symptoms and Diagnostic Category Assignments (Other Symptoms)		ABC_HSR_SYMP7	
44.	Listing of Liver Event Information for RUCAM Score		LIVER6	
45.	Listing of Extension Period Liver Event Information for RUCAM Score (Extension Switch Population)			W128
46.	Listing of Liver Biopsy Details		LIVER7	
47.	Listing of Extension Period Liver Biopsy Details (Extension Switch Population)			W128
48.	Listing of Liver Imaging Details		LIVER8	
49.	Listing of Extension Period Liver Imaging Details (Extension Switch Population)			W128
50.	Listing of Past and Current Liver Disease Medical Conditions			
51.	Listing of Past and Current Liver Disease Medical Conditions (Extension Switch Population)			W128
52.	Listing of Serology Results from Liver Event Follow-up			

Number	Title	Details/ Comments	IDSL/TST ID	Report
53.	Listing of Serology Results from Extension Period Liver Event Follow-up (Extension Switch Population)			W128
54.	Listing of Adverse Events Potentially Related to Torsades de Pointes		AE8	
55.	Listing of ECG Values for Subjects with Adverse Events Potentially Related to Torsades de Pointes		EG3	
56.	Listing of AST, ALT, Alkaline Phosphatase, and Total Bilirubin Laboratory Data for Subjects with On-Treatment ALT at Least Two Times the ULN			
57.	Listing of Extension Period AST, ALT, Alkaline Phosphatase, and Total Bilirubin Laboratory Data for Subjects with Extension Period On-Treatment ALT at Least Two Times the ULN (Extension Switch Population)			W128
58.	Listing of Grade 2 or higher Injection Site Reaction AE			
59.	Listing of Grade 2 or higher Extension Period Injection Site Reaction AEs (Extension Switch Population)			W128
60.	Listing of Patient Profile for Subjects Who Experienced Cardiovascular Event			
61.	Listing of All Liver Chemistry Data for Subjects Meeting Hepatobiliary Laboratory Abnormality Criteria at Any Post-Baseline Emergent Visit			
62.	Listing of All Liver Chemistry Data for Subjects Meeting Hepatobiliary Laboratory Abnormality Criteria at Any Extension Period Visit			W128
63.	Listing of Each Subject's Maximum ALT and Maximum Bilirubin			
64.	Listing of Each Subject's Maximum ALT and Maximum Bilirubin during the Extension Period (Extension Switch Population)			W128
65.	Listing of Investigational Product Exposure Data for Subject Receiving Oral Bridging			
66.	Listing of Investigational Product Exposure Data for Subject Receiving Oral Bridging during the Extension Period (Extension Switch Population)			W128
67.	Patient Profile of Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)			
68.	Patient Profile of Myocardial Infarction (MI)			

17.2.4. Health Outcome – Week 32/48/96

The ITT-ME Population will be used, except where noted.

17.2.4.1. Tables

Number	Title	Details/Comments	IDSL/TST ID	Report
1.	Summary of Individual Response of Injection Site Area Symptom from Diary Card by Visit and Overall			W32/W48
2.	Summary of Home Treatment for Injection Area Symptom as Reported in Diary Card			W32/W48
3.	Summary of Cardiovascular Activity, Strength Training and Other Strenuous Activity			W32/W48
4.	Summary of Total Weekly Duration for Cardiovascular Activity, Strength Training and Other Strenuous Activity			W32/W48
5.	Summary of HIV Treatment Satisfaction Questionnaire HIVTSQ(s) Individual Item Scores by Visit			
6.	Summary of HIV Treatment Satisfaction Questionnaire HIVTSQ(c) Individual Item Scores by Visit			W32/W48
7.	Summary of HIV Treatment Satisfaction Questionnaire HIVTSQ(s) Total Score by Visit			
8.	Summary of HIV Treatment Satisfaction Questionnaire HIVTSQ(c) Total Score by Visit			W32/W48
9.	Summary of HIV Medication Questionnaire (HIVMQ) Individual Item by Visit			
10.	Summary of HIV Medication Questionnaire (HIVMQ) Item D, E and F Score by Visit			
11.	Summary of HIV Medication Questionnaire (HIVMQ) Individual Item by Visit - Combined Score for CAB LA + RPV LA	New		W96

Number	Title	Details/Comments	IDSL/TST ID	Report
12.	Summary of HIV Medication Questionnaire (HIVMQ) Item D, E and F Score by Visit - Combined Score for CAB LA + RPV LA	New		W96
13.	Summary and Statistical Analysis of HIV Treatment Satisfaction Questionnaire HIVTST(s) Updated Total Score by Visit - Observed Case Dataset	New		W96
14.	Summary and Statistical Analysis of HIV Treatment Satisfaction Questionnaire HIVTST(s) Individual Item Score by Visit - Observed Case Dataset	New		W96

17.2.4.2. Figures

Number	Title	Details/Comments	IDSL/TST ID	Report
1.	Mean Plot of Injection Area Symptom Score by Day from Daily Dairy Card			W32/W48
2.	Median Plot of Injection Area Symptom Score by Day from Daily Dairy Card			W32/W48
3.	Bar Chart of HIV Treatment Satisfaction Questionnaire HIVTSQ(s) Mean Total Score by Visit			
4.	Bar Chart of HIV Treatment Satisfaction Questionnaire HIVTSQ(s) Mean Total Score by Visit - Updated Total Score by Visit			W96
5.	Bar Chart of HIV Treatment Satisfaction Questionnaire HIVTSQ(c) Mean Total Score by Visit			W32/W48
6.	Bar Char of HIV Medication Questionnaire Mean Score by Visit and Medication	Item d,e, f		

17.2.4.3. Other Listings

Number	Title	Details/Comments	IDSL/TST ID	Report
69.	Listing of Daily Diary Card For Symptoms at Injection Area			
70.	Listing of Subject's Exercise Habits			
71.	Listing of HIV Treatment Satisfaction Questionnaire HIVTSQ(s)			
72.	Listing of HIV Treatment Satisfaction Questionnaire HIVTSQ(c)			
73.	Listing of HIV Medication Questionnaire			

17.2.5. PK - Week 32/48/96/128

The PK Concentration Population will be used, except where noted.

17.2.5.1. Tables

Number	Title	Details/Comments	IDSL/ TST ID	Report
1.	Summary of Plasma GSK1265744 PK Concentration-Time Data by Treatment and Visit	ING112276 Table 9.2	PKCT1	W32/W48
2.	Summary of Plasma GSK1265744 PK Concentration-Time Data by Treatment and Visit from Week 100 to Week 128 (Extension Switch Population)			W128
3.	Summary of Plasma TMC278 PK Concentration-Time Data by Treatment and Visit	ING112276 Table 9.2	PKCT1	W32/W48
4.	Summary of Plasma TMC278 PK Concentration-Time Data by Treatment and Visit from Week 100 to Week 128 (Extension Switch Population)			W128
5.	Summary of Derived Plasma GSK1265744 PK Parameters by Treatment and Subgroup		PKPT4	W32/W48
6.	Summary of Plasma TMC278 PK Parameters by Treatment and Subgroup	ING112276 Table 9.3	PKPT4	W32/W48
7.	Summary of Results of Steady State Assessment			W32/W48
8.	Summary of Results of Steady State Assessment – Evaluable Concentrations			W32/W48
9.	Summary of Evaluable Plasma GSK1265744 PK Concentration-Time Data by Treatment and Visit			W32/W48
10.	Summary of Evaluable Plasma TMC278 PK Concentration-Time Data by Treatment and Visit			W32/W48
11.	Summary of Plasma GSK1265744 PK Concentration (ug/mL) -Time Data by Treatment and Visit – Included Log-transformed Statistics			W32/W48
12.	Summary of Extension Period Plasma GSK1265744 PK Concentration (ug/mL) -Time Data by Treatment and Visit– Included Log-transformed Statistics (Extension Switch Population)			W128

Number	Title	Details/Comments	IDSL/ TST ID	Report
13.	Summary of Plasma TMC278 PK Concentration (ng/mL) -Time Data by Treatment and Visit – Included Log-transformed Statistics			W32/W48
14.	Summary of Extension Period Plasma TMC278 PK Concentration (ug/mL) -Time Data by Treatment and Visit – Included Log-transformed Statistics (Extension Switch Population)			W128
15.	Summary of Evaluable Plasma GSK1265744 PK Concentration (ug/mL)-Time Data by Treatment and Visit – Included Log-transformed Statistics			W32/W48
16.	Summary of Extension Period Evaluable Plasma GSK1265744 PK Concentration (ug/mL) -Time Data by Treatment and Visit Statistics – Included Log-transformed Statistics (Extension Switch Population)			W128
17.	Summary of Evaluable Plasma TMC278 PK Concentration (ng/mL) -Time Data by Treatment and Visit – Included Log-transformed Statistics			W32/W48
18.	Summary of Extension Period Evaluable Plasma TMC278 PK Concentration (ug/mL) -Time Data by Treatment and Visit – Included Log-transformed Statistics (Extension Switch Population)			W128
19.	Summary of Derived Plasma GSK1265744 PK Parameters by Treatment and Exercise Habit Assessment Subgroups			W32/W48
20.	Summary of Derived Plasma TMC278 PK Parameters by Treatment and Exercise Habit Assessment Subgroups			W32/W48
21.	Summary of Long-Term Follow-up Period Plasma GSK1265744 PK Concentration (ug/mL) -Time Data by Treatment and Visit – Included Log-transformed Statistics	By arm and IM subtotal		W96
22.	Summary of Long-Term Follow-up Period Plasma TMC278 PK Concentration (ng/mL) -Time Data by Treatment and Visit – Included Log-transformed Statistics	By arm and IM subtotal		W96
23.	Summary of Evaluable Long-Term Follow-up Period Plasma GSK1265744 PK Concentration (ug/mL) -Time Data by Treatment and Visit – Included Log-transformed Statistics	By arm and IM subtotal		W96
24.	Summary of Evaluable Long-Term Follow-up Period Plasma TMC278 PK Concentration (ng/mL) -Time Data by Treatment and Visit – Included Log-transformed Statistics	By arm and IM subtotal		W96

17.2.5.2. Figures

Number	Title	Details/Comments	IDSL/TST ID	Report
1.	Individual Plasma GSK1265744 Concentration-Time Plots (Linear and Semi-Log)		PKCF1	W32/W48
2.	Individual Extension Period Plasma GSK1265744 Concentration Time Plots from (Linear and Semi-Log) – Extension Switch Population			W128
3.	Individual Plasma TMC278 Concentration-Time Plots (Linear and Semi-Log)		PKCF1	W32/W48
4.	Individual Extension Period Plasma TMC278 Concentration Time Plots (Linear and Semi-Log) – Extension Switch Population			W128
5.	Mean (SD) Plasma GSK1265744 Concentration-Time Plots (Linear and Semi-Log)	ING112276 Figure 9.2	PKCF2	W32/W48
6.	Median Plasma GSK1265744 Concentration-Time Plots (Linear and Semi-Log)	ING112276 Figure 9.3	PKCF3	W32/W48
7.	Mean (SD) Plasma TMC278 Concentration-Time Plots (Linear and Semi-Log)		PKCF2	W32/W48
8.	Median Plasma TMC278 Concentration-Time Plots (Linear and Semi-Log)		PKCF3	W32/W48
9.	Mean (SD) Evaluable Plasma GSK1265744 Concentration-Time Plots (Linear and Semi-Log)	ING112276 Figure 9.2	PKCF2	W32/W48
10.	Median Evaluable Plasma GSK1265744 Concentration-Time Plots (Linear and Semi-Log)	ING112276 Figure 9.3	PKCF3	W32/W48
11.	Mean (SD) Evaluable Plasma TMC278 Concentration-Time Plots (Linear and Semi-Log)		PKCF2	W32/W48
12.	Median Evaluable Plasma TMC278 Concentration-Time Plots (Linear and Semi-Log)		PKCF3	W32/W48
13.	Mean (SD) Evaluable Plasma GSK1265744 Concentration-Time Plots (Semi-Log)			W32/W48
14.	Mean (SD) Extension Period Evaluable Plasma GSK1265744 Concentration-Time Plots (Semi-Log) – Extension Switch Population			W128
15.	Mean (SD) Evaluable Plasma TMC278 Concentration-Time Plots (Semi-Log)			W32/W48
16.	Mean (SD) Extension Period Evaluable Plasma TMC278 Concentration-Time Plots (Semi-Log) – Extension Switch Population			W128

17.2.5.3. ICH Listings

Number	Title	Details/Comments	IDSL/TST ID	Report
24.	Listing of Plasma GSK1265744 PK Concentration-Time Data	ING112276 Listing 9.1	PKCL1	W32/W48
25.	Listing of Extension Period Plasma GSK1265744 PK Concentration-Time Data (Extension Switch Population)			W128
26.	Listing of Plasma TMC278 PK Concentration-Time Data		PKCL1	W32/W48
27.	Listing of Extension Period Plasma TMC278 PK Concentration-Time Data (Extension Switch Population)			W128
28.	Listing of Derived Plasma GSK1265744 PK Parameters	ING112276 Listing 9.2	PKPL1	W32/W48
29.	Listing of Derived Plasma TMC278 PK Parameters	ING112276 Listing 9.2	PKPL1	W32/W48
30.	Listing of Plasma GSK1265744 PK Concentration-Time Data (Safety Long-Term Follow-up Period Population)	New	PKCL1	W96
31.	Listing of Plasma TMC278 PK Concentration-Time Data (Safety Long-Term Follow-up Period Population)	New	PKCL1	W96

17.2.6. PK/PD- Week 32/48/96/128

17.2.6.1. Tables

Number	Title	Details/Comments	IDSL/TST ID	Report
1.	Summary of Logistic Regression of MSDF Response at Week X and Plasma GSK1265744 and TMC278 PK Parameters			W32/W48
2.	Summary of Logistic Regression of Virologic Failure (MSDF) at Week X and Plasma GSK1265744 and TMC278 PK Parameters			W32/W48
3.	Summary of Pearson's Correlations (P-values) of CD4+ Change from Baseline and Plasma GSK1265744 and TMC278 PK Parameters -- Maintenance Period			W32/W48
4.	Summary of Pearson's Correlations (p-values) of Maintenance Period On-Treatment Safety Parameters and Log-transformed Plasma GSK1265744 and TMC278 PK Parameters	Optional display		
5.	Summary of Logistic Regression of Maintenance Period On-Treatment AEs of Special Interest from Selected System Organ Class and Plasma GSK1265744 and TMC278 PK Parameters	Optional display		

17.2.6.2. PK/PD Figures

Number	Title	Details/Comments	IDSL/TST ID	Report
1.	Box plot Plasma GSK1265744 and TMC278 PK Parameters by MSDF Response and PDVF at Week X			W32/W48
2.	Median GSK1265744 Extension Period Conc-Time Profiles for W128 Successes and Snapshot Failures with Individual Profiles for Failures	Extension Switch Population		W128
3.	Median TMC278 Extension Period Conc-Time Profiles for W128 Successes and Snapshot Failures with Individual Profiles for Failures	Extension Switch Population		W128
4.	Troughs for GSK1265744 for Week 128 Non-failures and Failures	Extension Switch Population		W128
5.	Troughs for TMC278 for Week 128 Non-failures and Failures	Extension Switch Population		W128

17.2.7. Virology- Week 32/48/96/128

17.2.7.1. Tables

Number	Title	Details/Comments	IDSL/TST ID	Report
1.	Summary of the Prevalence of On-treatment INI Mutations – Maintenance Period	PDVF Genotypic Population		
2.	Summary of the Prevalence of Extension Period On-treatment INI Mutations	PDVF Genotypic Extension Switch Population		W128
3.	Summary of the Prevalence of Treatment Emergent INI Mutations – Maintenance Period	PDVF Genotypic Population		
4.	Summary of the Prevalence of Extension Period Treatment Emergent INI Mutations	PDVF Genotypic Extension Switch Population		W128
5.	Summary of the Prevalence of On-treatment Major Mutations of Other Classes – Maintenance Period	PDVF Genotypic Population		

Number	Title	Details/Comments	IDSL/TST ID	Report
6.	Summary of the Prevalence of Extension Period Major Mutations of Other Classes	PDVF Genotypic Extension Switch Population		W128
7.	Summary of the Prevalence of Treatment Emergent Major Mutations of Other Classes– Maintenance Period	PDVF Genotypic Population		
8.	Summary of the Prevalence of Extension Period Treatment Emergent Major Mutations of Other Classes	PDVF Genotypic Extension Switch Population		W128
9.	Summary of On-treatment Phenotype by Phenotypic Cutoff – Maintenance Period	PDVF Phenotypic Population		
10.	Summary of Extension Period On-treatment Phenotype by Phenotypic Cutoff	PDVF Phenotypic Extension Switch Population		W128
11.	Summary of On-Treatment Phenotype: Number of Drugs to Which Subjects are Resistant – Maintenance Period	PDVF Phenotypic Population		
12.	Summary of Extension Period On-Treatment Phenotype: Number of Drugs to Which Subjects are Resistant	PDVF Phenotypic Extension Switch Population		W128
13.	Summary of On-treatment Susceptibility to GSK1265744 and TMC278 – Maintenance Period	PDVF Phenotypic Population		
14.	Summary of On-treatment Susceptibility to GSK1265744 and TMC278 – Extension Period	PDVF Phenotypic Extension Switch Population		W128
15.	Summary of On-treatment Change from Baseline in Susceptibility to GSK1265744 and TMC278 – Maintenance Period	PDVF Phenotypic Population		
16.	Summary of On-treatment Change from Baseline in Susceptibility to GSK1265744 and TMC278 – Extension Period	PDVF Phenotypic Extension Switch Population		W128
17.	Listing of Genotypic Mutation Data at All Timepoints	PDVF Genotypic Population		
18.	Listing of Phenotypic Data at All Timepoints	PDVF Phenotypic Population		

17.2.7.2. Other Listings

Number	Title	Details/Comments	IDSL/TST ID	Report
32.	Listing of Genotypic Mutation Data at All Timepoints	PDVF Genotypic Extension Switch Population		W128
33.	Listing of Phenotypic Mutation Data at All Timepoints	PDVF Genotypic Extension Switch Population		W128
34.	Listing of Genotypic Mutation Data at Baseline and On-treatment	PDVF Genotypic Population		
35.	Listing of Treatment Emergent Genotypic Mutations	PDVF Genotypic Population		
36.	Listing of Treatment Emergent Genotypic Mutations during the Extension Period	PDVF Genotypic Extension Switch Population		W128
37.	Listing of All Genotypic Mutation Data	Intent-to-Treat Exposed Population		
38.	Listing of All Genotypic Mutation Data during the Extension Period	Extension Switch Population		W128
39.	Listing of Phenotypic Data at Baseline and On-treatment	PDVF Phenotypic Population		
40.	Listing of Phenotypic Data during the Extension Period	Extension Switch Population		W128
41.	Listing of Replication Capacity	PDVF Phenotypic Population		
42.	Listing of Replication Capacity	PDVF Genotypic Extension Switch Population		W128

17.3. Table of Contents for Data Display Specifications – Week 160

17.3.1. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	ITT-ME	ES1	Summary of Subject Accountability: Maintenance and Extension Period Conclusion Records (Randomized Q8W/Q4W)	W96 Table 6.1003.	W160
2.	ITT-ME	HIV_ES1	Summary of Subject Accountability: Withdrawal/Permanent Discontinuation of Investigational Product by Visit – Maintenance and Extension Period (Randomized Q8W/Q4W)	W96 Table 6.1002	W160
3.	ITT-E	ES4	Summary of Subject Disposition at Each Study Epoch	W96 Table 6.1006	W160
4.	ITT-E	ES5	Summary of Reasons for Withdrawal at Each Epoch	W96 Table 6.1007, follow the groups from Table 6.1006	W160
5.	ITT-E	NS1	Summary of Number of Subjects by Country and Site ID		W160
6.	Extension Switch	ES1	Summary of Subject Accountability: Extension Period Conclusion Record (Extension Switch Population)	W96 Table 6.1004	W160
7.	Extension Switch	HIV_ES1	Summary of Subject Accountability: Withdrawal/Permanent Discontinuation of Investigational Product by Visit - Extension Period (Extension Switch Population)		W160
Protocol Deviation					
8.	ITT-ME	DV1	Summary of Important Protocol Deviations During the Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
9.	Extension Switch	DV1	Summary of Important Protocol Deviations During the Extension Period (Extension Switch Population)		W160

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Population Analysed					
10.	All Subjects Screened		Summary of Study Populations	Add PDVF genotypic and phenotypic maintenance exposed, PDVF genotypic and phenotypic ES population W96 Table 6.1010	W160
11.	ITT-ME	SP2	Summary of Protocol Deviations Leading to Exclusion from the Per-Protocol ITT-ME Population (Randomized Q8W/Q4W)		W160
12.	Extension Switch	SP2	Summary of Protocol Deviations Leading to Exclusion from the Per-Protocol Extension Switch Population		W160
Demographic and Baseline Characteristics					
13.	ITT-ME	DM1	Summary of Demographic Characteristics	Please use Table 6.1010 as an example for treatment groups and remove the first 2 columns	W160
14.	ITT-ME	DM5	Summary of Race and Racial Combinations		W160
15.	ITT-ME	DM6	Summary of Race and Racial Combinations Details		W160
16.	ITT-ME	DM11	Summary of Age Ranges		W160
Prior and Concomitant Medications					
17.	ITT-ME	MH1	Summary of Current Medical Conditions	Please use Table 6.1010 as an example for treatment groups and remove the first 2 columns	W160
18.	ITT-ME	MH1	Summary of Past Medical Conditions	Please use Table 6.1010 as an example for treatment groups and remove the first 2 columns	W160
19.	ITT-ME	CM1	Summary of Concomitant Medication During Treatment by Ingredient ATC Level 1 – Maintenance and Extension Period (Randomized Q8W/Q4W)		W160

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
20.	ITT-ME	CM1b	Summary of Concomitant Medication by Combination Term ATC Level 1 – Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
21.	ITT-ME	CM8	Summary of Concomitant Medication Ingredient Combinations – Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
22.	Extension Switch	CM1	Summary of Concomitant Medication During Treatment by Ingredient ATC Level 1 – Extension Period (Extension Switch Population)		W160
23.	Extension Switch	CM1b	Summary of Concomitant Medication by Combination Term ATC Level 1 – Extension Period (Extension Switch Population)		W160
24.	Extension Switch	CM8	Summary of Concomitant Medication Ingredient Combinations – Extension Period (Extension Switch Population)		W160
Exposure and Treatment Compliance					
25.	ITT-ME		Summary of Extent of Exposure to Investigational Product – Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
26.	Extension Switch		Summary of Extent of Exposure to Investigational Product – Extension Period (Extension Switch Population)		W160

17.3.2. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Insert Endpoint Category					
1.	ITT-ME		Summary of Study Outcomes (<50 copies/mL) at Week 160 – Snapshot (MSDF) Analysis (Randomized Q8W/Q4W)		W160
2.	PP-ME		Summary of Study Outcomes (<50 copies/mL) at Week 160 – Snapshot (MSDF) Analysis for the Per-Protocol Randomized Q8W/Q4W Population	If PP-ME Population comprises less than 95% of the ITT-ME Population (randomized Q8W/Q4W)	W160
3.	ITT-ME		Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit during the Maintenance and Extension Period - Snapshot (MSDF) Analysis (Randomized Q8W/Q4W)	Up to Week 160	W160
4.	ITT-ME		Summary of Study Outcomes (<200 copies/mL) at Week 160 – Snapshot (MSDF) Analysis(Randomized Q8W/Q4W)		W160
5.	ITT-ME		Proportion of Subjects with Plasma HIV-1 RNA <200 copies/mL by Visit during the Maintenance and Extension Period - Snapshot (MSDF) Analysis (Randomized Q8W/Q4W)	Up to Week 160	W160
6.	ITT-ME		Cumulative Proportion of Subjects with Protocol Defined Virologic Failure by Visit - Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
7.	ITT-ME		Distribution of Quantitative Plasma HIV-1 RNA Results at Suspected and Confirmation of Protocol Defined Virologic Failure - Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
8.	ITT-ME		Summary of CD4+ Cell Count (cells/mm^3) by Visit – Maintenance and Extension Period (Randomized Q8W/Q4W)	Show baseline/Week-20, Day 1, W32, W48 and W96 + Extension	W160

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
9.	ITT-ME		Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit – Maintenance and Extension Period (Randomized Q8W/Q4W)	Induction baseline (study baseline)	W160
10.	ITT-ME		Summary of CD4+ / CD8+ Cell Count Ratios by Visit (Observed Case)	Show baseline/Week-20, W-4. Day 1, Week 32, Week 48 and Week 96.	W160
11.	ITT-ME		Summary of Change from Baseline in Plasma HIV-1 RNA (log10 copies/mL) by Visit (Randomized Q8W/Q4W)	Show baseline/Week-20, Day 1, W32, W48 and W96 + Extension	W160
12.	ITT-ME	HIV1	Summary of HIV-1 Associated Conditions Including Recurrences -Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
13.	ITT-ME	HIV1	Summary of HIV-1 Associated Conditions Excluding Recurrences -Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
14.	ITT-ME	HIV2	Summary of HIV-1 Associated Conditions Progression of HIV Disease – Maintenance and Extension Period (Randomized Q8W/Q4W Arms)		W160
15.	ITT-ME		Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit (Observed Case Analysis) Maintenance and Extension Period (Randomized Q8W/Q4W)	Include all visits available at the time of analysis	W160
16.	Extension Switch		Summary of Study Outcomes (<50 copies/mL) at Week 160 – Snapshot (MSDF) Analysis (Extension Switch Population)		W160
17.	PP-ES		Summary of Study Outcomes (<50 copies/mL) at Week 160 – Snapshot (MSDF) Analysis for the Per-Protocol Extension Switch Population	If PP-ES Population comprises less than 95% of the Extension Switch Population	W160
18.	Extension Switch		Proportion of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit during the Extension Period - Snapshot (MSDF) Analysis (Extension Switch Population)	Up to Week 160	W160

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
19.	Extension Switch		Summary of Study Outcomes (<200 copies/mL) at Week 160 – Snapshot (MSDF) Analysis (Extension Switch Population)		W160
20.	Extension Switch		Proportion of Subjects with Plasma HIV-1 RNA <200 copies/mL by Visit during the Extension Period - Snapshot (MSDF) Analysis	Up to Week 160	W160
21.	Extension Switch		Cumulative Proportion of Subjects with Extension Period Protocol Defined Virologic Failure by Visit (Extension Switch Population)		W160
22.	Extension Switch		Distribution of Quantitative Plasma HIV-1 RNA Results at Suspected and Confirmation of Extension Period Protocol Defined Virologic Failure (Extension Switch Population)		W160
23.	Extension Switch		Summary of CD4+ Cell Count (cells/mm^3) by Visit - Extension Period (Extension Switch Population)	See Week128 Table 7.1009	W160
24.	Extension Switch		Summary of Change from Baseline in CD4+ Cell Count (cells/mm^3) by Visit - Extension Period (Extension Switch Population)	Baseline is last value up to and including the date of first extension injection	W160
25.	Extension Switch		Summary of Change from Baseline in Plasma HIV-1 RNA (log10 copies/mL) by Visit (Extension Switch Population)	Baseline is last value up to and including the date of first extension injection	W160
26.	Extension Switch	HIV1	Summary of HIV-1 Associated Conditions Including Recurrences - Extension Period (Extension Switch Population)		W160
27.	Extension Switch	HIV1	Summary of HIV-1 Associated Conditions Excluding Recurrences - Extension Period (Extension Switch Population)		W160

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
28.	Extension Switch	HIV2	Summary of HIV-1 Associated Conditions Progression of HIV Disease - Extension Period (Extension Switch Population)		W160
29.	Extension Switch		Proportion of Subjects with Extension Period Plasma HIV-1 RNA <50 copies/mL by Visit - Observed Case Analysis) (Extension Switch Population)	Include all visits available at the time of analysis	W160

17.3.3. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Insert Endpoint Category					
1.	ITT-ME		Proportion (95% CI) of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit during the Maintenance and Extension Period– Snapshot Analysis (Randomized Q8W/Q4W)	W96 Figure 7.1001, start from Day 1	W160
2.	ITT-ME		Proportion (95% CI) of Subjects with Virologic Failure by Visit during the Maintenance and Extension Period – Snapshot Analysis (Randomized Q8W/Q4W)	W96 Figure 7.1004, start from Day 1	W160
3.	ITT-ME		Individual Plasma HIV-1 RNA (log10 copies/mL) Profiles by Visit during the Maintenance and Extension Period (Randomized Q8W/Q4W)	W96 Figure 7.1002, start from Baseline	W160
4.	Extension Switch		Proportion (95% CI) of Subjects with Plasma HIV-1 RNA <50 copies/mL by Visit during the Extension Period – Snapshot Analysis (Extension Switch Population)	W128 Figure 7.1001	W160

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.	Extension Switch		Proportion (95% CI) of Subjects with Virologic Failure by Visit during the Extension Period – Snapshot Analysis (Extension Switch Population)	W128 Figure 7.1002	W160
6.	Extension Switch		Individual Plasma HIV-1 RNA (log10 copies/mL) Profiles by Visit during the Extension Period (Extension Switch Population)	W128 Figure 7.1003, use Pink background to indicate Non Responders based on Week 160 Snapshot	W160

17.3.4. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
1.	Safety Maintenance		Summary of All Maintenance and Extension Period On-treatment Adverse Events by Overall Frequency (Randomized Q8W/Q4W)		W160
2.	Safety Maintenance	AE5 or AE5b	Summary of All On-Treatment Adverse Events by System Organ Class and Maximum Toxicity – Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
3.	Safety Maintenance		Summary of Common (>=3%) Grade 2-4 Maintenance and Extension Period Adverse Events by Overall Frequency (Randomized Q8W/Q4W)	3% of any arm	W160

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.	Safety Maintenance		Summary of Common (>=5%) Maintenance and Extension Period Non-Serious Adverse Event by System Organ Class and Preferred Term - Number of Subjects and Occurrences (Randomized Q8W/Q4W)	5% of any arm	W160
5.	Safety Maintenance		Summary of Grade 3/4 Maintenance and Extension Period On-treatment Adverse Events by Overall Frequency (Randomized Q8W/Q4W)		W160
6.	Safety Maintenance		Summary of Grade 3/4 Maintenance and Extension Period On-treatment Non Injection Site Reaction Related Adverse Events by Overall Frequency (Randomized Q8W/Q4W)		W160
7.	Safety Maintenance		Summary of Drug-Related Maintenance and Extension Period On-treatment Adverse Events by Overall Frequency (Randomized Q8W/Q4W)		W160
8.	Safety Maintenance		Summary of All Drug-Related On-treatment Adverse Events by System Organ Class and Maximum Toxicity – Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
9.	Safety Maintenance		Summary of Maintenance and Extension Period Common (>=3%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency (Randomized Q8W/Q4W)	3% of any arm	W160
10.	Extension Switch		Summary of All Extension Period On-treatment Adverse Events by Overall Frequency (Extension Switch Population)		W160
11.	Extension Switch		Summary of Extension Period On-treatment Adverse Events by System Organ Class and Maximum Toxicity (Extension Switch Population)		W160
12.	Extension Switch		Summary of Common (>=3%) Grade 2-4 Extension Period Adverse Events by Overall Frequency (Extension Switch Population)	3% of total subjects.	W160

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
13.	Extension Switch		Summary of Common (>=5%) Extension Period Non-Serious Adverse Event by System Organ Class and Preferred Term - Number of Subjects and Occurrences (Extension Switch Population)	5% of total subjects	W160
14.	Extension Switch		Summary of Grade 3/4 Extension Period On-treatment Adverse Events by Overall Frequency (Extension Switch Population)		W160
15.	Extension Switch		Summary of Grade 3/4 Extension Period On-treatment Non Injection Site Reaction Related Adverse Events by Overall Frequency (Extension Switch Population)		W160
16.	Extension Switch		Summary of Drug-Related Extension Period On-treatment Adverse Events by Overall Frequency (Extension Switch Population)		W160
17.	Extension Switch		Summary of Drug-Related Extension Period On-treatment Adverse Events by System Organ Class and Maximum Toxicity (Extension Switch Population)		W160
18.	Extension Switch		Summary of Extension Period Common (>=3%) Drug-Related Grade 2-4 Adverse Events by Overall Frequency (Extension Switch Population)	3% of total subjects	W160
19.	Safety Long-Term Follow Up		Summary of All Long-term Follow-up Period Adverse Events by Overall Frequency (Safety Long-Term Follow-up Population)	Including all subjects in LTFU	W160
20.	Safety Long-Term Follow-Up		Summary of Long-Term Follow-up Period Drug-Related Adverse Events by Overall Frequency (Safety Long-Term Follow-Up Population)	Including all subjects in LTFU	W160

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Serious and Other Significant Adverse Events					
21.	Safety Maintenance		Summary of Maintenance and Extension Period Serious On-treatment Adverse Events by Overall Frequency (Randomized Q8W/Q4W)		W160
22.	Safety Maintenance		Summary of Maintenance and Extension Period Serious Adverse Events by System Organ Class and Preferred Term - Number of Subjects and Occurrences (Randomized Q8W/Q4W)		W160
23.	Safety Maintenance		Summary of Maintenance and Extension Period Drug-Related Serious Adverse Events by Overall Frequency (Randomized Q8W/Q4W)		W160
24.	Safety Maintenance	AE1	Summary of Maintenance and Extension Period Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class (Randomized Q8W/Q4W)		W160
25.	Safety Maintenance		Summary of Maintenance and Extension Period Drug-Related Grade 3/4 Adverse Events by Overall Frequency (Randomized Q8W/Q4W)		W160
26.	Safety Maintenance		Summary of Maintenance and Extension Period Drug-related Grade 3/4 Non Injection Site Reaction Related Adverse Events by Overall Frequency (Randomized Q8W/Q4W)		W160
27.	Extension Switch		Summary of Extension Period Serious On-treatment Adverse Events by Overall Frequency (Extension Switch Population)		W160
28.	Extension Switch		Summary of Extension Period Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)Extension Switch Population		W160

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
29.	Extension Switch		Summary of Extension Period Drug-Related Serious Adverse Events by Overall Frequency (Extension Switch Population)		W160
30.	Extension Switch	AE1	Summary of Extension Period Adverse Events Leading to Withdrawal/Permanent Discontinuation of Investigational Product by System Organ Class (Extension Switch Population)		W160
31.	Extension Switch		Summary of Extension Period Drug-Related Grade 3/4 Adverse Events by Overall Frequency (Extension Switch Population)		W160
32.	Extension Switch		Summary of Extension Period Drug-related Grade 3/4 Non Injection Site Reaction Related Adverse Events by Overall Frequency (Extension Switch Population)		W160
33.	Safety Long-Term Follow-Up		Summary of Long-Term Follow-up Period Serious Adverse Events by Overall Frequency (Safety Long-Term Follow-up Population)		W160
Injection Site Reaction Adverse Events					
34.	Safety Maintenance		Summary of Event-Level Injection Site Reaction Adverse Events - Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
35.	Safety Maintenance		Summary of Overall and Common Subject-Level Characteristics of Injection Site Reaction Adverse Events - Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
36.	Safety Maintenance		Summary of Overall and Common Injection Site Reaction Adverse Events by Visit and Maximum Severity - Maintenance and Extension Period (Randomized Q8W/Q4W)		W160

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
37.	Safety Maintenance		Summary of Total Number of Injection Site Reaction Adverse Events by Visit - Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
38.	Safety Maintenance		Summary of Overall and Common Subject-Level Characteristics of Injection Site Reaction Adverse Events by Needle Length - Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
39.	Safety Maintenance		Summary of Event-Level Maintenance and Extension Period Injection Site Reaction Adverse Events - GSK1265744 (Randomized Q8W/Q4W)		W160
40.	Safety Maintenance		Summary of Overall and Common Subject-Level Characteristics of Maintenance and Extension Period Injection Site Reaction Adverse Events - GSK1265744 (Randomized Q8W/Q4W)		W160
41.	Safety Maintenance		Summary of Overall and Common Maintenance and Extension Period Injection Site Reaction Adverse Events by Visit and Maximum Severity - GSK1265744 (Randomized Q8W/Q4W)		W160
42.	Safety Maintenance		Summary of Total Number of Maintenance and Extension Period Injection Site Reaction Adverse Events by Visit - GSK1265744 (Randomized Q8W/Q4W)		W160
43.	Safety Maintenance		Summary of Event-Level Maintenance and Extension Period Injection Site Reaction Adverse Events - TMC278 (Randomized Q8W/Q4W)		W160

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
44.	Safety Maintenance		Summary of Overall and Common Subject-Level Characteristics of Maintenance and Extension Period Injection Site Reaction Adverse Events - TMC278 (Randomized Q8W/Q4W)		W160
45.	Safety Maintenance		Summary of Overall and Common Maintenance and Extension Period Injection Site Reaction Adverse Events by Visit and Maximum Severity -TMC278 (Randomized Q8W/Q4W)		W160
46.	Safety Maintenance		Summary of Total Number of Maintenance and Extension Period Injection Site Reaction Adverse Events by Visit - TMC278 (Randomized Q8W/Q4W)		W160
47.	Extension Switch		Summary of Event-Level Injection Site Reaction Adverse Events – Extension Period (Extension Switch Population)		W160
48.	Extension Switch		Summary of Overall and Common Subject-Level Characteristics of Injection Site Reaction Adverse Events - Extension Period (Extension Switch Population)		W160
49.	Extension Switch		Summary of Overall and Common Injection Site Reaction Adverse Events by Visit and Maximum Severity - Extension Period (Extension Switch Population)		W160
50.	Extension Switch		Summary of Total Number of Injection Site Reaction Adverse Events by Visit - Extension Period (Extension Switch Population)		W160

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
51.	Extension Switch		Summary of Overall and Common Subject-Level Characteristics of Injection Site Reaction Adverse Events by Needle Length - Extension Period (Extension Switch Population)		W160
52.	Extension Switch		Summary of Event-Level Extension Period Injection Site Reaction Adverse Events - GSK1265744 (Extension Switch Population)		W160
53.	Extension Switch		Summary of Overall and Common Subject-Level Characteristics of Extension Period Injection Site Reaction Adverse Events - GSK1265744 (Extension Switch Population)		W160
54.	Extension Switch		Summary of Overall and Common Extension Period Injection Site Reaction Adverse Events by Visit and Maximum Severity - GSK1265744 (Extension Switch Population)		W160
55.	Extension Switch		Summary of Total Number of Extension Period Injection Site Reaction Adverse Events by Visit - GSK1265744 (Extension Switch Population)		W160
56.	Extension Switch		Summary of Event-Level Extension Period Injection Site Reaction Adverse Events - TMC278(Extension Switch Population)		W160
57.	Extension Switch		Summary of Overall and Common Subject-Level Characteristics of Extension Period Injection Site Reaction Adverse Events - TMC278 (Extension Switch Population)		W160

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
58.	Extension Switch		Summary of Overall and Common Extension Period Injection Site Reaction Adverse Events by Visit and Maximum Severity - TMC278 (Extension Switch Population)		W160
59.	Extension Switch		Summary of Total Number of Extension Period Injection Site Reaction Adverse Events by Visit - TMC278 (Extension Switch Population)		W160
Laboratory: Chemistry					
60.	Safety Maintenance	LB1	Summary of Chemistry Changes from Baseline by Visit – Maintenance and Extension Period (Randomized Q8W/Q4W)	Display Baseline/W-20, Day1, W32, W48, W96 + Extension Period	W160
61.	Safety Maintenance		Summary of Maximum Maintenance and Extension Period Treatment Emergent Clinical Chemistry Toxicities (Randomized Q8W/Q4W) – Relative to Maintenance Baseline	See main RAP for definition of "emergent".	W160
62.	Safety Maintenance		Summary of Maximum Maintenance and Extension Period Treatment Emergent Clinical Chemistry Toxicities (Randomized Q8W/Q4W) – Relative to Induction Baseline		W160
63.	Safety Maintenance		Summary of Changes in Clinical Chemistry Baseline Toxicity to Maximum Maintenance and Extension Period On-Treatment Toxicity - Parameters of Special Interest (Randomized Q8W/Q4W) – Relative to Maintenance Baseline	Baseline is last value up to and including Maintenance Day 1 Parameters of Special Interest: AST, ALT, ALP and BILT	W160
64.	Safety Maintenance		Summary of Changes in Clinical Chemistry Baseline Toxicity to Maximum Maintenance and Extension Period On-Treatment Toxicity - Parameters of Special Interest (Randomized Q8W/Q4W) – Relative to Induction Baseline		W160

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
65.	Extension Switch	LB1	Summary of Chemistry Changes from Extension Baseline by Visit – Extension Period (Extension Switch Population)	Baseline is last value up to and including the date of first extension injection. W128 Table 8.1030	W160
66.	Extension Switch		Summary of Maximum Extension Period Treatment Emergent Clinical Chemistry Toxicities (Extension Switch Population)		W160
67.	Extension Switch		Summary of Changes in Clinical Chemistry Baseline Toxicity to Maximum Extension Period On-Treatment Toxicity - Parameters of Special Interest (Extension Switch Population)	W128 Table 8.1034	W160
Laboratory: Hematology					
68.	Safety Maintenance	LB1	Summary of Hematology Changes from Baseline by Visit – Maintenance and Extension Period (Randomized Q8W/Q4W)	Display Baseline/W-20, Day1, W32, W48, W96 + Extension Period	W160
69.	Safety Maintenance		Summary of Maximum Maintenance and Extension Period Treatment Emergent Hematology Toxicities (Randomized Q8W/Q4W) – Relative to Maintenance Baseline		W160
70.	Safety Maintenance		Summary of Maximum Maintenance and Extension Period Treatment Emergent Hematology Toxicities (Randomized Q8W/Q4W) – Relative to Induction Baseline		W160
71.	Extension Switch	LB1	Summary of Hematology Changes from Baseline by Visit – Extension Period (Extension Switch Population)	Baseline is last value up to and including the date of first extension injection	W160
72.	Extension Switch		Summary of Maximum Extension Period Treatment Emergent Hematology Toxicities (Extension Switch Population)		W160

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Urinalysis					
73.	Safety Maintenance	LB1	Summary of Urine Concentration Changes from Baseline by Visit – Maintenance and Extension Period (Randomized Q8W/Q4W)	Display Baseline/W-20, Day 1, W32, W48, W96 + Extension	W160
74.	Safety Maintenance	UR3/LB2	Summary of Post-Baseline Emergent Urinalysis Dipstick Results Maintenance and Extension Period (Randomized Q8W/Q4W) – Relative to Induction Baseline		W160
75.	Safety Maintenance	UR3/LB2	Summary of Post-Baseline Emergent Urinalysis Dipstick Results Maintenance and Extension Period (Randomized Q8W/Q4W) – Relative to Maintenance Baseline		W160
76.	Extension Switch	LB1	Summary of Urine Concentration Changes from Baseline by Visit – Extension Period (Extension Switch Population)	W128 Table 8.1035	W160
77.	Safety Maintenance	UR3/LB2	Summary of Extension Period Post-Baseline Emergent Urinalysis Dipstick Results (Extension Switch Subjects)	Extension Baseline	W160
Laboratory: Hepatobiliary (Liver)					
78.	Safety Maintenance	LIVER10	Summary of Maintenance and Extension Period Hepatobiliary Laboratory Abnormalities (Randomized Q8W/Q4W)	W96 Table 8.1072	W160
79.	Extension Switch	LIVER10	Summary of Extension Period Hepatobiliary Laboratory Abnormalities (Extension Switch Population)	W128 Table 8.1037	W160

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ECG					
80.	Safety Maintenance	EG2	Summary of Change from Baseline in ECG Values by Visit – Maintenance and Extension Period (Randomized Q8W/Q4W)	Display Baseline/W-20, Day 1, W32, W48, W96 + Extension	W160
81.	Safety Maintenance		Summary of QTc Values by Category – Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
82.	Safety Maintenance		Summary of Change from Baseline QTc Values by Category – Maintenance and Extension Period (Randomized Q8W/Q4W)	Display Baseline/W-20, Day 1, W32, W48, W96 + Extension	
83.	Extension Switch	EG2	Summary of Change from Baseline in ECG Values by Visit – Extension Period (Extension Switch Population)	Baseline is last value before the date of first extension injection. W128 Table 8.1040	W160
84.	Extension Switch		Summary of QTc Values by Category – Extension Period (Extension Switch Population)		W160
85.	Extension Switch		Summary of Change from Baseline QTc Values by Category – Extension Period (Extension Switch Population)		W160
Vital Signs					
86.	Safety Maintenance	VS1	Summary of Change from Baseline in Vital Signs by Visit – Maintenance and Extension Period (Randomized Q8W/Q4W)	Display Baseline/W-20, Day 1, W32, W48, W96 + Extension	W160
87.	Extension Switch	VS1	Summary of Change from Baseline in Vital Signs by Visit – Extension Period (Extension Switch Population)	Extension baseline. W128Table 8.1042	W160

17.3.5. Safety Figures

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.	Safety Maintenance		Figure of Onset, Duration, and Severity of Overall and Common Maintenance and Extension Period Injection Site Reaction Adverse Events by Maximum Grade: GSK744 LA or TMC278 LA (Randomized Q8W/Q4W)		W160
2.	Safety Maintenance		Figure of Incidence of Overall and Common Maintenance and Extension Period Injection Site Reaction Adverse Events - GSK 744 LA or TMC278 LA (Randomized Q8W/Q4W)		W160
3.	Safety Maintenance		Figure of Incidence of Overall and Common Grade 3-4 Maintenance and Extension Period Injection Site Reaction Adverse Events - GSK 744 LA or TMC278 LA (Randomized Q8W/Q4W)		W160
4.	Safety Maintenance		Scatter Plots of Maximum Maintenance and Extension Period On-Treatment vs. Baseline for ALT (Randomized Q8W/Q4W)	Baseline is last value up to and including date of first maintenance injection. See W128 Figure 8.1001	W160
5.	Safety Maintenance		Matrix Plot of Maximum Maintenance and Extension Period On-treatment Liver Chemistries (Randomized Q8W/Q4W)	See W128 Figure 8.1002	W160
6.	Safety Maintenance		Liver Chemistry Profile Plots for Subjects with Elevation during the Maintenance and Extension Period by Study Day (Randomized Q8W/Q4W)	Maintenance study day	W160
7.	Safety Maintenance		Scatter Plot of Maximum Maintenance and Extension Period On-Treatment Value: ALT vs. BILT (Randomized Q8W/Q4W)	See W128 Figure 8.1004	W160
8.	Extension Switch		Figure of Onset, Duration, and Severity of Overall and Common Extension Period Injection Site Reaction Adverse Events by Maximum Grade: GSK744 LA or TMC278 LA (Extension Switch Population)		W160

Safety: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
9.	Extension Switch		Figure of Incidence of Overall and Common Extension Period Injection Site Reaction Adverse Events - GSK 744 LA or TMC278 LA (Extension Switch Population)		W160
10.	Extension Switch		Figure of Incidence of Overall and Common Grade 3-4 Extension Period Injection Site Reaction Adverse Events - GSK 744 LA or TMC278 LA (Extension Switch Population)		W160
11.	Extension Switch		Scatter Plots of Maximum Extension Period On-Treatment vs. Baseline for ALT (Extension Switch Population)	Baseline is last value up to and including date of first extension injection. See W128 Figure 8.1001	W160
12.	Extension Switch		Matrix Plot of Maximum Extension Period On-treatment Liver Chemistries (Extension Switch Population)		W160
13.	Extension Switch		Liver Chemistry Profile Plots for Subjects with Elevation during the Extension Period by Study Day (Extension Switch Population)	Extension Study day	W160
14.	Extension Switch		Scatter Plot of Maximum Extension Period On-Treatment Value: ALT vs. BILT (Extension Switch Population)		W160

17.3.6. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Insert Endpoint Category					
1.	PK Population	PKCT1	Summary of Maintenance Period Plasma GSK1265744 PK Concentration (ug/mL) -Time Data by Treatment and Visit – Including Log-transformed Statistics	Day 1 to W96, by 3 groups: Q8W,Q4W and Oral	W160
2.	PK Population	PKCT1	Summary of Maintenance Period Plasma TMC278 PK Concentration (ug/mL) -Time Data by Treatment and Visit – Including Log-transformed Statistics		W160
3.	PK Population	PKCT1	Summary of Evaluable Maintenance Period Plasma GSK1265744 PK Concentration (ug/mL) -Time Data by Treatment and Visit – Including Log-transformed Statistics		W160
4.	PK Population	PKCT1	Summary of Evaluable Maintenance Period Plasma TMC278 PK Concentration (ug/mL) -Time Data by Treatment and Visit – Including Log-transformed Statistics		W160

17.3.7. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Insert Endpoint Category					
1.	PK	PKCF1	Individual Maintenance Period Plasma GSK1265744 Concentration Time Plots (Linear and Semi-Log)		W160
2.	PK	PKCF1	Individual Maintenance Period Plasma TMC278 Concentration Time Plots (Linear and Semi-Log)		W160
3.	PK	PKCF2	Mean(SD) Evaluable Maintenance Period Plasma GSK1265744 Concentration Time Plots (Linear and Semi-Log)		W160
4.	PK	PKCF2	Mean(SD) Evaluable Maintenance Period Plasma TMC278 Concentration Time Plots (Linear and Semi-Log)		W160

17.3.8. Virology Tables

Virology Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Insert Endpoint Category					
1.	PDVF Genotypic Maintenance Exposed	See Table 9.1002 from W96	Summary of the Prevalence of Treatment Emergent Known INI Mutations at the time of PDVF (Randomized Q8W/Q4W)		W160
2.	PDVF Genotypic Maintenance Exposed	See Table 9.1004 from W96	Summary of the Prevalence of Treatment Emergent Major Mutations of Other Classes at the time of PDVF (Randomized Q8W/Q4W)		W160
3.	PDVF Phenotypic Maintenance Exposed	See Table 9.1005 from W96	Summary of Phenotype by Phenotypic Cutoff at the Time of PDVF (Randomized Q8W/Q4W)		W160
4.	PDVF Phenotypic Maintenance Exposed	See Table 9.1006 from W96	Summary of Phenotype: Number of Drugs to Which Subjects are Resistant (Randomized Q8W/Q4W)		W160
5.	PDVF Phenotypic Maintenance Exposed	See Table 9.1007 from W96	Summary of Susceptibility to GSK1265744 and TMC278 – Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
6.	PDVF Phenotypic Maintenance Exposed	See Table 9.1008 from W96	Summary of Change from Baseline in Susceptibility to GSK1265744 and TMC278 (Randomized Q8W/Q4W)		W160

Virology Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
7.	PDVF Genotypic Extension Switch		Summary of the Prevalence of Treatment Emergent INI Mutations at the time of PDVF (PDVF Genotypic Extension Switch Population)	Note: treatment emergence is always derived by comparing to study baseline prior to induction	W160
8.	PDVF Genotypic Extension Switch		Summary of the Prevalence of Treatment Emergent Major Mutations of Other Classes at the time of PDVF (PDVF Genotypic Extension Switch Population)		W160
9.	PDVF Phenotypic Extension Switch		Summary of Phenotype by Phenotypic Cutoff at the time of PDVF (Extension Switch Population)		W160
10.	PDVF Phenotypic Extension Switch		Summary of Phenotype: Number of Drugs to Which Subjects are Resistant (Extension Switch Population)		W160
11.	PDVF Phenotypic Extension Switch		Summary of Susceptibility to GSK1265744 and TMC278 (Extension Switch Population)		W160
12.	PDVF Phenotypic Extension Switch		Summary of Change from Baseline in Susceptibility to GSK1265744 and TMC278 (Extension Switch Population)		W160

17.3.9. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	ITT-ME	ES2	Listing of Reasons for Study Withdrawal	W96 Listing 6.1002	W160
Protocol Deviations					
2.	ITT-ME	DV2	Listing of Important Protocol Deviations During the Maintenance and Extension Period (Randomized Q8W/Q4W)		W160
3.	Extension Switch	DV2	Listing of Important Protocol Deviations During the Extension Period (Extension Switch Population)		W160
Demographic and Baseline Characteristics					
4.	ITT-ME	DM2	Listing of Demographic Characteristics	Include 5 groups: Q8W, Q4W, Oral/Q8W, Oral/Q4W, Oral/no Extension	W160
5.	ITT-ME	DM9	Listing of Race	Include 5 groups: Q8W, Q4W, Oral/Q8W, Oral/Q4W, Oral/no Extension	W160
Prior and Concomitant Medications					
6.	ITT-ME	CM2	Listing of Concomitant Medications	W96 Listing 6.1013	W160
Exposure and Treatment Compliance					
7.	ITT-ME		Listing of Investigational Product Exposure Data	See Listing 8.1001 from W96	W160
Efficacy					
8.	ITT-ME		Listing of Quantitative Plasma HIV-1 RNA Data	See Listing 7.1001 from W96	W160
9.	ITT-ME		Listing of Study Outcome (<50 copies/mL) at Week 160 – Snapshot (MSDF)	See Listing 7.1002 from W96	W160

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
10.	ITT-ME		Listing of Study Outcome (<200 copies/mL) at Week 160 – Snapshot (MSDF)	See Listing 7.1003 from W96	W160
11.	Safety LTFU		Listing of Plasma HIV-1 RNA Data for Subjects in Long-term Follow up	New listing. See Listing 3 from pub_2017_01	W160
Safety: Adverse Events					
12.	Safety Maintenance		Listing of All Adverse Events	See Listing 8.1002 from W96	W160
13.	Safety Maintenance	AE7	Listing of Subject Numbers for Individual Adverse Events	See Listing 8.1006 from W96	W160
14.	Safety Maintenance	PREG1a	Listing of Subjects Who Became Pregnant during the Study	See Listing 8.1007 from W96	W160
Safety: Serious and Other Significant Adverse Events					
15.	Safety Maintenance		Listing of Fatal Adverse Events		W160
16.	Safety Maintenance		Listing of Non-Fatal Serious Adverse Events		W160
17.	Safety Maintenance		Listing of Reasons for Considering an AE as Serious		W160
18.	Safety Maintenance	AE8	Listing of Adverse Events Leading to Permanent Discontinuation of Investigational Product and/or Withdrawal from the Study	W96 Listing 8.1005	W160
Safety: Hepatobiliary (Liver)					
19.	Safety Maintenance	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events	5 groups, see Listing 8.1012 from W96	W160
20.	Safety Maintenance	MH2	Listing of Substance Use for Subjects with Liver Stopping Events	5 groups, see Listing 8.1013 from W96	W160

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Safety: ECG					
21.	Safety Maintenance		Listing of ECG Values	5 groups, see Listing 8.1008 from W96	W160
22.	Safety Maintenance	EG3	Listing of ECG Values for Subjects with a Value of Potential Clinical Concern	5 groups, see Listing 8.1019 from W96	W160
23.	Safety Maintenance	EG5	Listing of ECG Findings	5 groups, see Listing 8.1010 from W96	W160
Safety: Vital Signs					
24.	Safety Maintenance	VS4	Listings of Vital Signs	5 groups, see Listing 8.1011 from W96	W160
Pharmacokinetic					
25.	PK	PKCL1	Listing of Plasma GSK1265744 PK Concentration - Time Data		W160
26.	PK	PKCL1	Listing of Plasma TMC278 PK Concentration - Time Data		W160

17.3.10. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Study Population					
27.	All Screened		Listing of study Populations	W96 Listing 6.1007. Add PDVF genotypic and phenotypic maintenance exposed, PDVF genotypic and phenotypic ES population (remove on-treatment geno. Resist and pheno. Resist)	W160
28.	ITT-ME		Listing of Investigational Product Accountability	W96 Listing 6.1012	W160
29.	ITT-ME		Listing of Concomitant and Post-Treatment Antiretroviral Therapy	W96 Listing 6.1016	W160
30.	ITT-ME		Listing of Subjects with Changes in Concomitant Antiretroviral Therapy	W96 Listing 6.1017	W160
31.	ITT-ME		Listing of Current and Past Medical Conditions at Baseline	W96 Listing 6.1014	W160
32.	ITT-ME		Listing of Relationship Between ATC Level 1, Ingredient and Verbatim Text		W160
33.	ITT-ME		Listing of Relationship Between ATC Level 4, Combination, and Verbatim Text for ART		W160
Efficacy					
34.	ITT-ME		Listing of CD4+ Cell Count Data	W96 Listing 7.1004	W160
35.	ITT-ME		Listing of HIV-1 Associated Conditions	W96 Listing 7.1005	W160
36.	ITT-ME		Listing of Subjects with Protocol Defined Virologic Failure	W96 Listing 7.1007	W160

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
37.	ITT-ME		Listing of Quantitative Plasma HIV-1 RNA Data for Subjects Classified as Having 'data in window >50' at any Maintenance or Extension Period Visit based on the Snapshot Classification (Randomized Q8W/Q4W)	W96 Listing 7.1009	W160
38.	Extension Switch		Listing of Quantitative Plasma HIV-1 RNA Data for Subjects Classified as Having 'data in window >50' at any Extension Period Visit based on the Snapshot Classification (Extension Switch)	W128 Listing 7.1007	W160
39.	ITT-ME		Listing of Quantitative Plasma HIV-1 RNA Data for Subjects with HIV-1 RNA >= 50 c/mL at any time during the Maintenance Period or Extension Period	W96 Listing 7.1010	W160
Safety					
40.	Safety Maintenance	AE2	Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		W160
41.	Safety Maintenance	LB5	Listing of Clinical Chemistry Laboratory Data for Subjects with Grade 3/4 Maintenance and Extension Period Treatment-Emergent Toxicities Relative to Maintenance Baseline (Randomized Q8W/Q4W)	ICH E3	W160
42.	Safety Maintenance	LB5	Listing of Clinical Chemistry Laboratory Data for Subjects with Grade 3/4 Maintenance and Extension Period Treatment-Emergent Toxicities Relative to Induction Baseline (Randomized Q8W/Q4W)		W160
43.	Safety Maintenance	LB5	Listing of Hematology Laboratory Data for Subjects with Grade 3/4 Maintenance and Extension Period Treatment-Emergent Toxicities Relative to Maintenance Baseline (Randomized Q8W/Q4W)		W160

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
44.	Safety Maintenance	LB5	Listing of Hematology Laboratory Data for Subjects with Grade 3/4 Maintenance and Extension Period Treatment-Emergent Toxicities Relative to Induction Baseline (Randomized Q8W/Q4W)		W160
45.	Safety Maintenance	UR2a	Listing of Urinalysis Data for Subjects with Grade 3/4 Maintenance and Extension Period Treatment-Emergent Toxicities (Randomized Q8W/Q4W) – Relative to Maintenance Baseline		W160
46.	Safety Maintenance	UR2a	Listing of Urinalysis Data for Subjects with Grade 3/4 Maintenance and Extension Period Treatment-Emergent Toxicities (Randomized Q8W/Q4W) – Relative to Induction Baseline		W160
47.	Safety Maintenance	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting	Week 96 Table 8.1068, 5 treatment groups	W160
48.	Safety Maintenance	LIVER13	Listing of Subjects Meeting Hepatobiliary Laboratory Abnormality Criteria during the Maintenance or Extension Period	Updated Display Standard, Week 96 Table 8.1069, 5 treatment groups	W160
49.	Safety Maintenance	LIVER6	Listing of Liver Event Information for RUCAM Score	W96 Listing 8.1026, 5 treatment groups	W160
50.	Safety Maintenance	LIVER7	Listing of Liver Biopsy Details		W160
51.	Safety Maintenance	LIVER8	Listing of Liver Imaging Details		W160
52.	Safety Maintenance		Listing of Past and Current Liver Disease Medical Conditions		W160

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
53.	Safety Maintenance		Listing of Serology Results Liver Event Follow-up		W160
54.	Safety Maintenance		Listing of AST, ALT, Alkaline Phosphatase, and Total Bilirubin Laboratory Data for Subjects with Maintenance or Extension Period On-Treatment ALT at Least Two Times the ULN (Randomized Q8W/Q4W)		W160
55.	Safety Maintenance		Listing of Grade 2 or higher Maintenance or Extension Period Injection Site Reaction AEs	W96 Listing 8.1034, 5 treatment groups	W160
56.	Safety Maintenance		Listing of Each Subject's Maximum ALT and Maximum Bilirubin during the Maintenance and Extension Period (Randomized Q8W/Q4W)	W96 Listing 8.1037	W160
57.	Safety Maintenance		Listing of Investigational Product Exposure Data for Subject Receiving Oral Bridging during the Maintenance or Extension Period	W96 Listing 8.1038, 5 treatment groups	W160
58.	Extension Switch	LB5	Listing of Clinical Chemistry Laboratory Data for Subjects with Grade 3/4 Extension Period Treatment-Emergent Toxicities (Extension Switch Population)	ICH E3	W160
59.	Extension Switch	LB5	Listing of Hematology Laboratory Data for Subjects with Grade 3/4 Extension Period Treatment-Emergent Toxicities (Extension Switch Population)	ICH E3	W160
60.	Extension Switch	UR2a	Listing of Urinalysis Data for Subjects with Grade 3/4 Extension Period Treatment-Emergent Toxicities (Extension Switch Population)		W160
61.	Extension Switch		Listing of AST, ALT, Alkaline Phosphatase, and Total Bilirubin Laboratory Data for Subjects with Extension Period On-Treatment ALT at Least Two Times the ULN (Extension Switch Population)		W160

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
62.	Extension Switch		Listing of Each Subject's Maximum ALT and Maximum Bilirubin during the Extension Period (Extension Switch)		W160
Virology					
63.	ITT-E		Listing of All Genotypic Mutation Data at All Time Points	By Treatment groups – Induction no maintenance, Q8W, Q4W,Oral/Q8W, Oral/Q4W, Oral/no extension, induction only, Use W96cdic Table 9.1009	W160
64.	ITT-E		Listing of All Phenotypic Mutation Data at All Time Points	By Treatment groups – Induction no maintenance, Q8W, Q4W,Oral/Q8W, Oral/Q4W, Oral/no extension, induction only. Use W96cdic Table 9.1010	W160
65.	PDVF Genotypic Maintenance Exposed		Listing of Treatment Emergent Genotypic Mutations at the time of PDVF (Randomized Q8W/Q4W)		W160
66.	PDVF Phenotypic Maintenance Exposed		Listing of Replication Capacity (Randomized Q8W/Q4W)	See Listing 9.1005 from W96	W160
67.	PDVF Genotypic Extension Switch		Listing of Treatment Emergent Genotypic Mutations at the time of PDVF (Extension Switch Population)		W160

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
68.	PDVF Phenotypic Extension Switch		Listing of Replication Capacity (Extension Switch Population)		W160

17.4. Data Display Specifications

Data display specifications are available upon request.

17.5. MSDF (Snapshot) Algorithm in Detail

Consider an arbitrary visit window, Week X. A subject's response (i.e., 'Virologic Success', 'Virologic Failure', or 'No Virologic Data at Week X') in that window is determined as follows:

- If there was a non-permitted change in background ART prior to Week X, then the subject is a Virologic Failure.

If there was a permitted change in background ART prior to Week X per protocol but prescribed while not suppressed (e.g., HIV-1 RNA ≥ 50 copies/mL based on last viral load at time of decision to switch), unless the decision to switch is documented as being on or before the first on-treatment visit where HIV-1 RNA is assessed., , then the subject is a Virologic Failure.

If there is a change in background ART during Week X, and the decision to make this change is after the first On-treatment HIV-1 RNA result, and

a. no HIV-1 RNA result is available during Week X prior to the change, then the subject is a Virologic Failure;

   there is at least one HIV-1 RNA result available during Week X prior to the change, then consider the latest such result:

   i. if <50 c/mL, then the subject is a Virologic Success;

   ii. if ≥50 c/mL, then the subject is a Virologic Failure.

If there is no change in background ART during Week X or such a change is decided on before the first On-treatment HIV-1 RNA result, and at least one HIV-1 RNA result is available during Week X, then consider the latest such result:

b. if <50 c/mL, then the subject is a Virologic Success;

c. if ≥50 c/mL, then the subject is a Virologic Failure.

If there is no change in background ART during Week X or such a change is decided on before the first On-treatment HIV-1 RNA result, and no HIV-1 RNA results are available during Week X:

d. if the subject has not withdrawn from the study prior to or during Week X, they are categorized as 'No Virologic Data at Week X', with a reason of 'Missing data during window but on study';

   if the subject was withdrawn from the study prior to or during Week X due to AE or death, they are categorized as 'No Virologic Data at Week X', with a reason of 'Discontinued due to AE or Death';

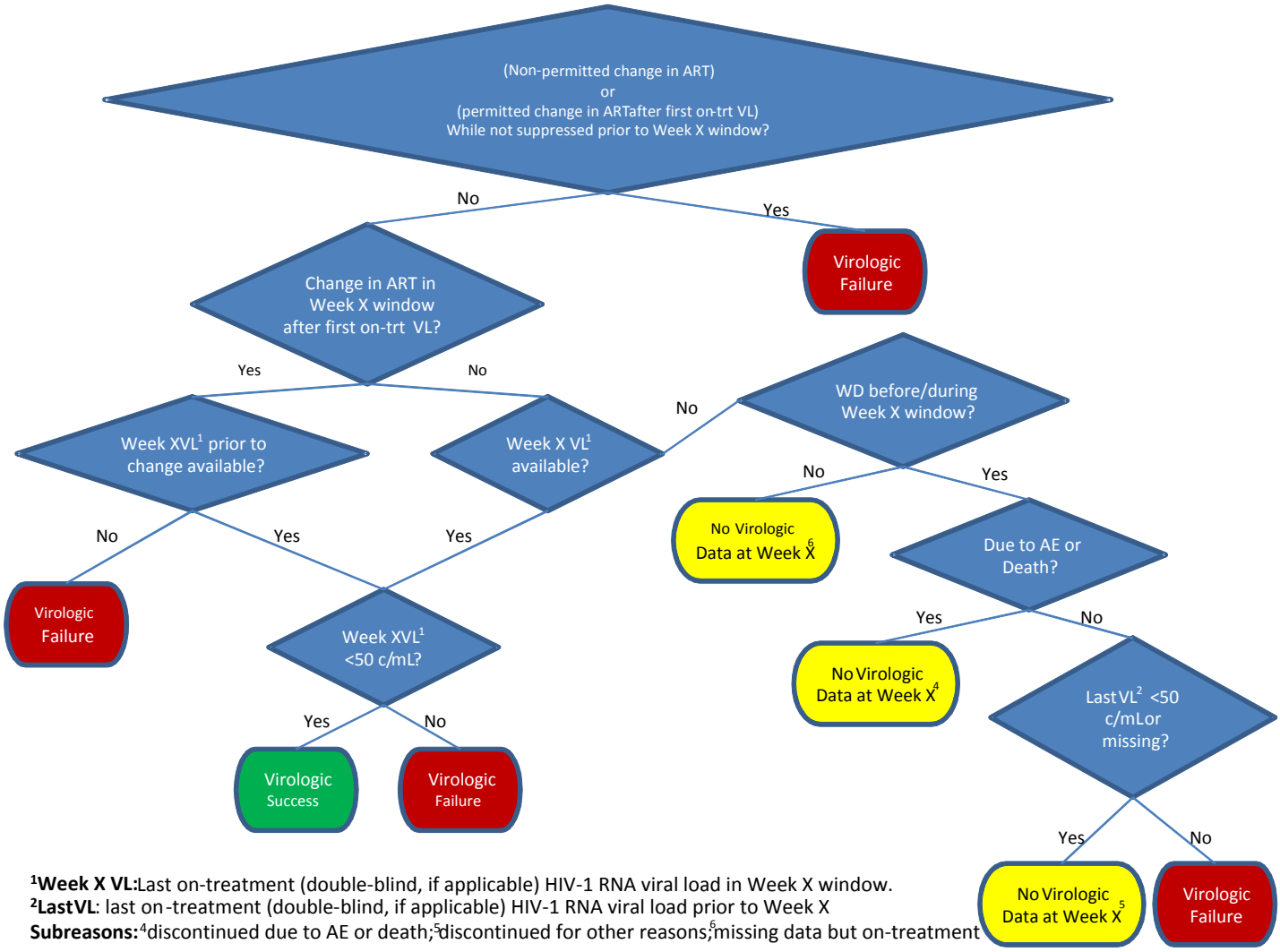
   otherwise, consider the subject's last available On-treatment HIV-1 RNA result:

iii. if <50 c/mL or no result is available, then the subject is categorized as 'No Virologic Data at Week X', with a reason of 'Discontinued for Other Reasons';

iv. if ≥50 c/mL, then the subject is a Virologic Failure.

To view a graphical representation of this algorithm, see Figure 4.

Figure 4 MSDF (Snapshot) Algorithm



[1]**Week X VL:**Last on-treatment (double-blind, if applicable) HIV-1 RNA viral load in Week X window.
[2]**LastVL**: last on-treatment (double-blind, if applicable) HIV-1 RNA viral load prior to Week X
Subreasons:[4]discontinued due to AE or death;[5]discontinued for other reasons;[6]missing data but on-treatment