Reporting and Analysis Plan

Study ID: APV20002

Official Title of Study: A 48 Week Phase II, Open-label, 2-cohort, Multicentre Study to Evaluate the Pharmacokinetics, Safety, Tolerability and Antiviral Activity of GW433908 and GW433908/RTV When Administered to HIV-1 Infected Protease Inhibitor (PI) Naïve and PI-Experienced Pediatric Subjects aged 4 weeks to <2 years.

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ABBREVIATIONS

3TC	Lamivudine, EPIVIR
AAG	alpha-1 acid glycoprotein
ABC	Abacavir, ZIAGEN
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase (SGPT)
ANOVA	analysis of variance
APV	Amprenavir
ART	antiretroviral therapy
AST	aspartate aminotransferase (SGOT)
ATC	Anatomical therapeutic chemical
ATV	Atazanavir
ATV/r	ATV boosted with RTV
AUC(0-τ)	area under the concentration versus time curve during a dosing interval, τ, at steady state
AUC(0-∞)	area under the plasma concentration versus time curve from time 0 and extrapolated to infinity
%AUCex	percent of AUC(0-∞) that is extrapolated beyond the last quantified concentration
AUC(0-t)	area under the plasma concentration versus time curve from time 0 to the time of the last quantifiable concentration
AUCτ,ss	AUC for the dosing interval at steady state
BID	twice daily
CD4+	helper-inducer T-lymphocyte surface antigen
Cavg	average concentration during the dosing interval at steady-state
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CL/F	apparent clearance of drug from plasma following extravascular administration
Cmax	maximum concentration
Cmax,ss	Cmax at steady state
CPMS	clinical pharmacology modelling and simulation
CRF	Case report form
CSR	Clinical study report
Cτ	concentration at the end of a dosing interval, τ, at steady state
CV	coefficient of variation for the arithmetic mean
CVb	coefficient of variation for the geometic mean
d4T	Stavudine
ddI	Didanosine
DLV	Delavirdine
DRV/r	Darunavir boosted with RTV
EFV	Efavirenz
ETV	Etravirine

FC	Fold Change
FDA	Food and Drug Administration (US)
FPV	Fosamprenavir, TELZIR, LEXIVA
FPV/RTV	FPV boosted with RTV, FPV/r
FR	Fold reduction
FSFV	First subject first visit
FTC	Emtricitabine
GLS	geometric least squares mean
GSK	Glaxo SmithKline
h	Hour
HDL	high density lipoprotein
HIV-1	human immunodeficiency virus type 1
IAS	International AIDS Society
IC50	Inhibitory Concentration, 50%
IDV	Indinavir
IDV/r	Indinavir boosted with RTV
ITT(E)	Intent-to-Treat Exposed
λz	terminal phase rate constant
LDL	low density lipoprotein
LFT	liver function test
LOCF	last observation carried forward
LOD	limit of detection
LPV/r	Lopinavir/Ritonavir
MSD=F	missing, switch or discontinuation equals failure
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mL	Millilitre
NFV	Nelfinavir, Viracept
NNRTI	non-nucleoside reverse transcriptase inhibitor
NRTI	nucleoside reverse transcriptase inhibitor
NVP	Nevirapine
Obs	Observed
OS	Oral suspension
PCR	polymerase chain reaction
PD	Pharmacodynamics
PI	protease inhibitor
PK	Pharmacokinetics
PR	Protease
RAP	Reporting Analysis Plan
RPV	Rilpivirine
RNA	Ribonucleic acid
RT	Reverse transcriptase
RTV	ritonavir, /r,
SAE	serious adverse event
SD	Standard deviation
SDV	single dose visit
SOP	Standard Operating Procedure
SQV	Saquinavir

SQV/r	Saquinavir boosted with RTV
t1/2	apparent plasma half-life
TAM	Thymidine analogue mutation
TFV	Tenofovir
tlag	lag time before observation of drug concentrations in plasma
TLOVR	time to loss of virologic response
tmax	first time of occurrence of Cmax
TPV	Tipranavir
ZDV	Zidovudine, RETROVIR

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COMBIVIR		SAS
EPIVIR		UNIX
LEXIVA		QUEST
RETROVIR		Winnonln
TELZIR		Monogram
TRIZIVIR		PhenoSense
VIRACEPT		UltraSensitive Monitor
ZIAGEN		Geneseq

1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to provide details of planned analyses and data displays for reporting the safety, antiviral response, global health outcome and virology results of study APV20002. These analyses will be used in study reports and publications.

The analyses detailed in this document are based on the latest version of the APV20002 protocol (Document Code GD2001/00007/12) issued on 20th Nov 2019. This is the twelfth amendment to the original protocol (Document Code GD2001/00007/00) issued on 20th September 2002 (see Section 2.1).

The original RAP is based on the standard operating procedure SOP_000000548383 (4.0) Development, Review and Approval of Reporting and Analysis Plans. It was written using the document standard DS-WWD-4000 v03 issued on 11th November 2005. It covered the analyses produced for the primary analysis at Week 48 and prior interim analyses. The original RAP included pharmacokinetic sampling assessments and Health Outcomes and Compliance questionnaires performed at the Week 48 visit or by the cut-off date of 05July2011. Virology analyses in the original analysis were censored to include only those subjects who had met confirmed virologic failure criteria by Week 48. The amended RAP will cover a subset of the endpoints to further describe the data collected after the Week 48 data cut-off for the primary analysis for the safety endpoints, the observed efficacy endpoint, a limited analysis of pharmacokinetic (PK) data collected after 05July2011 cut-off and the virology results for those subjects who met confirmed virologic failure criteria after 48 weeks. These results will be described in the abbreviated Clinical Study Report (CSR) that will be produced for the results collected after the 05July2011 cut-off for the Week 48 analysis.

In this document, fosamprenavir/GW433908 will be referred to as FPV, amprenavir as APV and ritonavir as RTV.

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

2.1. Study Objective(s)

APV20002 was planned to evaluate the PK, safety, tolerability and antiviral activity of FPV oral suspension (OS) when administered to HIV-1 infected protease inhibitor (PI)-naïve and PI-experienced pediatric subjects aged 4 weeks to <2 years. Enrolment into cohorts evaluating unboosted FPV was closed, and FPV was only administered in combination with low dose RTV (used as a pharmacokinetic enhancer). In addition to FPV/RTV, study participants also received two nucleoside reverse transcriptase inhibitors (NRTIs), where the choice of NRTIs was determined by the site physician, as part of their antiretroviral therapy (ART). Subjects in this study were enrolled into two age cohorts (Cohort 1: 6 months to <2 years, and Cohort 2: 4 weeks to <6 months) to determine the FPV/RTV dosage regimens for pediatric subjects at various stages of physiologic development. An abbreviated interim analysis with a cut-off date of March 31, 2006 was published in September 2006 [GlaxoSmithKline Document Number

RM2006/00360/00], while a 24 week analysis with a cut-off date of November 2011 was published in June 2011 [GlaxoSmithKline Document Number 2010N107734_01] and a 48-week analysis of data collected through 05July2011 [GlaxoSmithKline Document Number 2011N127273_00_01].

The APV20002 study included an optional extension phase for subjects enrolled in sites in South Africa as fosamprenavir oral suspension (FPV OS) was not commercially available in South Africa after the last enrolled subject reached 48 weeks on treatment on 05July2011, the cut-off for the Week 48 analysis to provide them with access to FPV OS. The most recent protocol amendment 12 was minor as it was implemented to provide additional RTV formulation treatment options for the South African subjects because the RTV manufacturer discontinued sale of the protocol mandated RTV oral solution. This amendment applied to those subjects enrolled in APV20002 as of November 1, 2019 at study sites in South Africa. The study is expected to end in March 2022, when the final subject will be withdrawn.

For this RAP amendment, as many of the primary and secondary objectives were met in the 48 week primary analysis, the final study analysis will focus on the incidence and frequency of adverse events and laboratory abnormalities, the virologic efficacy and immunologic impact of this ART regimen through the end of study (EoS), genotypic and phenotypic resistance in subjects who met protocol-defined virologic failure criteria after 48 weeks. All PK objectives were met through previous analyses. The additional PK data past 05July2011 (week 48 reporting) is less than 10% of the total pharmacokinetic (PK) data and were sparse samples taken for routine clinical follow-up. These data are not expected to change any of the conclusions drawn previously on the objectives, nor provide new insights into the PK of the investigated treatments. Therefore, instead of a full PK analysis, only summary statistics will be performed on the remaining PK data collected after 05July2011.

2.1.1. Primary Study Objectives

The bulleted primary study objectives were completed at the time of the Week 48 primary analysis, which included data collected up to the cut-off of 05July2011.

- To define the FPV/RTV twice daily (BID) dosage regimens which will provide target steady-state plasma APV exposure to HIV-1 infected paediatric subjects aged 4 weeks to <2 years
- To evaluate the safety and tolerability of FPV (deferred per amendment 5) and FPV/RTV when administered as a component of combination therapy in HIV-1 infected subjects aged 4 weeks to <2 years.

The safety and efficacy of FPV OS-containing ART continued to be evaluated for the subset of subjects who continued in the study after the 05July2011 data cut-off for the week 48 analysis. Safety events will be summarized in two groups: those reported cumulatively throughout the study and those reported after 05July2011 until study completion (EoS). Due to the small number of subjects (n=25) who continued in the study past 05July2011, a comparison will be made between the two groups to determine if any safety events were reported in both groups and these will be identified in the

report. All cumulative safety events will be listed for this study. As described previously, a full analysis of the PK data after the timepoint of 05July2011 (week 48 reporting) is not considered relevant and thus only summary statistics of drug concentrations collected after 05July2011will be included in the CSR.

2.1.2. Secondary Study Objectives

The bulleted secondary objectives have already been met and reported in week 48 CSR.

- The antiviral activity was evaluated for the on treatment population that completed 48 weeks of treatment in APV20002 and continues to receive FPV/RTV in combination with NRTI therapy
- The immunologic activity was evaluated for the on treatment population that completed 48 weeks of treatment in APV20002 and continued to receive FPV/RTV in combination with NRTI therapy up to the 48 week analysis data cut-off of 05July2011
- The systemic exposure to FPV was evaluated for the on treatment population that completed 48 weeks of treatment in APV20002 and continued to receive FPV/RTV in combination with NRTI therapy up to the 48 week analysis data cut-off of 05July2011
- Assessed plasma RTV $AUC_{\tau,ss,}$ $C_{max,ss}$ and $C_{\tau,ss}$ following multiple dose administration of FPV/RTV twice daily BID for samples obtained up to the 48 week analysis data cut-off of 05July2011
- Investigated the relationship of steady state plasma APV PK parameters to changes in plasma HIV-1 RNA concentrations, CD4+ percentages and / or the occurrence of adverse events for samples obtained up to the 48 week analysis data cut-off of 05July2011
- Assessed viral resistance patterns and compared these patterns with treatment outcome (where permissible by blood volumes) for subjects who met the definition of confirmed virologic failure after 48 weeks of treatment with FPV/RTV in combination with NRTI therapy

For the EoS report, the safety, efficacy and assessment of virologic failure for HIV-1 infected paediatric subjects who were 4 weeks to <2 years at study enrolment and treated with FPV/RTV in combination with NRTIs were evaluated until the subjects discontinued, completed the 48 weeks on treatment, or until the subjects reached 39 kilograms and were withdrawn from the study or at study closure (by not later than April 29, 2022).

2.2. Study Endpoint(s)

2.2.1. Primary Study Endpoints

The bulleted primary study endpoints were completed at the time of the Week 48 primary analysis:

- Plasma APV $AUC_{\tau,ss}$, $C_{max,ss}$ and $C_{\tau,ss}$ following multiple dose administration of FPV BID (deferred per amendment 5). This endpoint was removed along with closure of enrolment into the unboosted cohorts (Cohort 1 Arm B and Cohort 2 Arm B) per Protocol Amendment 10.
- Plasma APV $AUC_{\tau,ss}$, $C_{max,ss}$ and $C_{\tau,ss}$ following multiple dose administration of FPV/RTV twice daily (BID)
- The incidence and nature of adverse events, laboratory abnormalities, and treatment limiting toxicities
- Proportion of subjects who permanently discontinued FPV (deferred per amendment 5) or FPV/RTV due to adverse events

For the EoS report, safety endpoints as bulleted below will continue to be evaluated:

- The incidence and nature of adverse events, laboratory abnormalities, and treatment limiting toxicities will be evaluated for the subset of subjects who continued in the study after the 05July2011 data cut-off for the 48 Week data analysis.
- For the subset of subjects who continued in the study after the 05July2011 data cut-off for the 48 Week data analysis, the proportion of subjects who permanently discontinue FPV/RTV due to adverse events will be evaluated.

2.2.2. Secondary Study Endpoints

The original secondary endpoints were completed at the time of the Week 48 primary analysis:

- Proportions of subjects with plasma HIV-1 RNA levels < 400 copies/mL at each study visit
- Change from Baseline in plasma HIV-1 RNA at each study visit (absolute values and time-averaged)
- Proportion of subjects with ≥ 1.0 log10 decrease in plasma HIV-1 RNA at each study visit
- Change from Baseline in the percentage of CD4+ lymphocytes at each study visit (absolute values and time-averaged)
- Plasma FPV concentrations
- Plasma RTV $AUC_{\tau,ss}$, $C_{max,ss}$ and $C_{\tau,ss}$ following multiple dose administration of FPV/RTV BID
- Relationship of steady state plasma APV PK parameters to changes in plasma HIV-1 RNA concentrations, CD4+ percentages and / or the occurrence of adverse events
- Subject adherence, and parent/guardian perceptions of study medications
- Incidence of viral resistance (where permissible by blood volumes)

For the EoS analysis, these endpoints will be evaluated using the data obtained after 05July2011, the cut-off date for the Week 48 primary analysis:

- Proportions of subjects with plasma HIV-1 RNA levels < 400 copies/mL at each study visit
- Change from Baseline in plasma HIV-1 RNA at each study visit (absolute values and time-averaged)
- Change from Baseline in the percentage of CD4+ lymphocytes at each study visit (absolute values and time-averaged)
- Plasma FPV concentrations collected after the 05July2011 data lock will be summarized (mean and standard deviation, median and 95% percentiles).
- Incidence of viral mutations and phenotypic resistance patterns for subjects who met the protocol definition of confirmed virologic failure after Week 48.

2.3. Statistical Hypotheses

No formal statistical hypothesis testing will be performed in this EoS analysis. Only descriptive methods will be used in any analysis of the data obtained from this study after 05July2011.

3. STUDY DESIGN

APV20002 is an international, 48-week, Phase II, open-label, 2–cohort, multicentre study conducted in HIV-1 infected pediatric subjects 4 weeks to <2 years old. This study was conducted in seven centres, three in South Africa, two in Mexico and one each in Argentina and Portugal. Subjects successfully completing 48 weeks of therapy in APV20002 had the option to continue in the study with visits every 12 weeks until commercial supplies of FPV OS were available locally and paediatric dosing was approved in the relevant age groups. In countries where local availability was delayed or the drug was not yet available through national treatment programs, subjects could continue to receive FPV until they no longer derived clinical benefit, the carers/legal guardians withdrew consent or the subjects were discontinued according to prior agreements between GSK and the participating study sites regarding provision of ART.

As per Amendments 7 and 8, the approximate number of additional subjects required in APV20002 is illustrated in Table 1. Cohort 1 Arm A (FPV/RTV, 6 months to <2years) and Cohort 2 Arm A (FPV/RTV, 4 weeks to <6 months) were open in parallel. Cohort 1 Arm A and Cohort 2 Arm A recruited either PI-naïve or experienced subjects. Enrolment into Arm B (unboosted FPV cohorts 1 and 2) was closed and no subjects received unboosted FPV as per amendment 10 (effective 28-MAR-2011). Recruitment status as of the week 48 CSR is provided below in Table 1.

Dose recommendations have been modified in this and previous protocol amendments (3, 5, 7 and 8). The remaining evaluable PK data collected after 05July2011 will be analysed at the end of the study and will include subjects who have been on different dosing regimens.

Table 1 Recruitment Status for APV20002 – from Oct 2003 (FSFV) to 05 Jul 2011 (cutoff for 48 week CSR)

Age (yrs) Cohorts	No. of Subjects originally planned	Cumulative enrolment and current status[1]
1A 6months - <2yr PI-naïve/exp FPV/RTV (boosted)	12	**28** enrolled[2]
2A 4wks - <6mo PI-naïve/exp FPV/RTV (boosted)	12	**26** enrolled[2]

1. A total of 59 patients were enrolled but 5 were discontinued after receiving single dose of FPV; the total enrolled number of patients exceeds the original cohort target because of dose changes in previous amendments
Source data: Table 6.3 APV20002 48 week study report GSK Document 2011N127273_00

Cohort 1 Arm A (FPV/RTV, 6 months to <2years) and Cohort 2 Arm A (FPV/RTV, 4 weeks to <6 months) were open in parallel. Cohort 1 Arm A and Cohort 2 Arm A recruited either PI-naïve or experienced subjects.

Dose recommendations were modified in protocol amendments 3, 5, 7 and 8. The evaluable PK data for approximately 50 to 60 subjects was analysed at the Week 48 data lock (05July2011) and included subjects who were on different dosing regimens.

The initial group of subjects who were enrolled into the study underwent a single dose visit (SDV) before commencing multiple dosing with for example FPV/RTV at Baseline and were referred to as Arm A SDV. As per Amendments 5 and 7, no additional subjects were required to undergo SDV assessments.

For more details on the study design, please refer to Section 3 in the latest version of protocol, Protocol Amendment 12 [GlaxoSmithKline Document Number GD2001/00007/12].

4. PLANNED ANALYSES

Evaluation of APV PK following single dose administration of FPV and FPV/RTV was performed for the first 6-10 subjects enrolled in each cohort in order to provide individual dosage regimen recommendations to investigators, because APV had not been studied in children <2 years of age and data for other HIV-1 PIs has demonstrated that children <2 years require much higher mg/kg doses than older children and adults. In addition, it was possible to undertake expedited analysis of plasma APV, RTV and FPV on a case by case basis on PK trough samples collected to allow for dose regimen adjustment due to the physiological development with age.

4.1. Abbreviated Interim Analysis

An abbreviated interim analysis of APV20002 including data for subjects enrolled in Arm A was conducted and included as part of a regulatory submission. All data up to and including the 31st of March 2006 was included in the analysis and contained data through 48 Weeks for 10 subjects. The abbreviated interim analysis is included in the CSR [RM2006/00360/00] issued on 20th September 2006.

4.2. 24-Week Analysis

Data up to the cut-off date of 24th November 2010 was included in this analysis. This included 24 week safety, PK, and efficacy data for 54 subjects. The 24 week analysis is included in the CSR [GlaxoSmithKline Document Number 2010N107734_00] issued on June 8, 2011.

4.3. 48-Week Analysis

Data up to and including the 05July2011 cut-off date was included in the week 48 analysis. The Week 48 CSR was generated after the database was cleaned and included all subjects who had not withdrawn prior to week 48 and was issued April 24, 2012 [GlaxoSmithKline Document Number 2011N127273_00_01].

4.4. Final Analysis

A final analysis will be performed when all subjects discontinued, completed the 48 weeks on treatment, or until the subjects reached 39 kilograms and were withdrawn from the study or at study closure (by not later than April 29, 2022). This closeout appendix RAP will provide the details of planned analyses and data displays for APV20002 EoS reporting for the EoS CSR.

5. SAMPLE SIZE CONSIDERATIONS

The sample size of 48 subjects was selected as an appropriate number to allow an accurate description of plasma APV PK, safety and tolerability of FPV BID, Arm B (n=24 for PK and safety; enrolment closed per Amendment 10; effective 28Mar-2011] and FPV/RTV BID, Arm A (n=24 for PK and safety). Safety and tolerability assessment of the FPV/RTV BID regimen (Arm A) was assessed for the duration of the study or until a subject permanently discontinues the study drug.

6. GENERAL CONSIDERATIONS FOR DATA ANALYSES

This appendix RAP is written additionally to support the main RAP (effective on 29-SEP-2011). Since the primary analyses have been completed based on the main RAP, the present RAP is written to cover only analyses included in the final reporting. Only those definitions and derivations that have changed since previous interim analyses will be

included in the current RAP, i.e. for derivation of analysis windowing, how to deal with missing dates, definition of concomitant medications, etc. refer to the main RAP. This RAP summarizes only the key endpoints of interest for the final analysis and explains any deviations from the main RAP.

Since the analysis in the main RAP censored the virology data to include only those subjects who met the criteria for confirmed virologic failure by Week 48, additional descriptions of those analysis populations are included here for the EoS report.

7. ANALYSIS POPULATIONS

7.1. Safety Population

All subjects receiving FPV or FPV/RTV at any dose will be included in the safety population. Safety events will be summarized in two groups: those reported cumulatively throughout the study and those reported after 05July2011 until study completion (EoS). The EoS population continuing in the study following the July 5 2011 cut-off date will be the primary population for any safety analyses in this amended RAP and all cumulative safety events will be listed for this study.

7.2. Baseline Virology Population

All subjects enrolled into the study with data from Day 1 (Baseline) or Screening HIV Resistance Testing (Geneseq and PhenoSense, Monogram Biosciences Inc.) will be included in this population. This population will be used for the virology analysis.

7.3. Virological Failure Population

A specific comprehensive definition for virologic failure was not included in the original protocol. Therefore, to be consistent with current standard practice, for the Week 24 analysis virologic failure was defined as failure to achieve a plasma HIV-RNA value of < 400 copies/mL by Week 24 or two consecutive values of HIV-RNA rebound to ≥400 copies/mL after initially achieving a plasma HIV-RNA of <400 copies/mL. If a subject had a single viral load rebound ≥400 copies/mL at Week 24 and it was their last available visit and hence virological failure could not be confirmed, they were not included in the Week 24 Virological Failure Population. The Week 48 analysis included those subjects defined as virological failures in the Week 24 analysis along with subjects who had two consecutive values of HIV-RNA rebound to ≥400 copies/mL after achieving a plasma HIV-1 RNA of <400 copies/mL between Week 24 and Week 48. Therefore, if a subject had a single viral load rebound HIV-1 RNA ≥400 copies/mL at Week 48 and it was their last available visit so virological failure could not be confirmed, they were not included in the Virological Failure Population for the Week 48 CSR.

Plasma samples from subjects with plasma HIV-1 RNA >400 copies/mL, when available, were sent for HIV Resistance Testing (Geneseq and PhenoSense, Monogram Biosciences Inc.) if the subject had met the criteria for confirmed virologic failure together with the baseline samples for these subjects. Baseline samples may have been sent for HIV

Resistance Testing for some subjects at study start to assist investigators with selection of appropriate NRTI ART. Samples with plasma HIV-1 RNA >400 copies/ml were also sent for analysis at additional timepoints during the study at the request of investigators to aid patient management.

Since the confirmed virologic failure results presented in the Week 48 CSR were censored to include only subjects with confirmed virologic failure by Week 48, the EoS virology analysis will include summary tables for subjects who had two consecutive values of HIV-RNA ≥400 copies/mL after achieving a plasma HIV-1 RNA of <400 copies/mL at any time after Week 48 through the EoS. Subjects who met confirmed virologic failure criteria by Week 48 and were included in the Week 48 CSR will not be included in these EoS tables describing subsequent confirmed virologic failures and treatment emergent changes in drug resistance or resistance associated mutations. In the event that a subject had a single HIV-1 RNA value of ≥400 copies/mL at Week 48 and it was their last available visit at the July 5 2011 data cut-off so that virologic failure was unconfirmed and the subject had a second consecutive HIV-1 RNA ≥400 copies/mL at their next study visit, then the subject would be deemed a virological failure and the results for this subject will be included in the summary tables for Virological Failure Population for the EoS report. Treatment emergent resistance associated mutations and treatment emergent changes in phenotypic resistance will be calculated for subjects meeting confirmed virologic failure at any time after Week 48 and the EoS for all confirmed virologic failure subjects with baseline genotypic or phenotypic data. This will be the primary population for genotypic and phenotypic analyses. However, a disposition table will also summarize how many subjects met confirmed virologic failure criteria by Week 48 and how many additional subjects met this criterion after Week 48 through EoS.

7.4. Total Virology Population

All subjects with HIV resistance testing data will be included in this population, including those with genotypic and phenotypic data obtained post-baseline where the subject is not considered a virological failure. This population will be used for the listings of virology data for all subjects with genotypic and/or phenotypic data collected from study start through EoS.

7.5. Data Display Treatment and Other Sub-group Descriptors

In data displays, treatment groups, dose regimen groups and age groups will be identified as described in Table 2 and footnotes will be provided in the PK summary tables. All of the dose regimens will be summarised and listed, but only the regimens with n ≥6 subjects will be included in PK statistics treatment comparisons.

Table 2 Group Descriptors

Treatment Group	Descriptor	
FPV 30mg/kg single dose alone	FPV SD	
FPV 30mg/kg + RTV 6mg/kg single dose	FPV/RTV SD	
FPV/RTV BID	FPV/RTV BID	
Age Group		
6 months-<24 months at PK profile	6-<24m	
4week-<6months at PK profile	**1-<6m**	
Dose Group	**Description**	**Value**
FPV/RTV where FPV was dosed within 40.5-49.5mg/kg	FPV/RTV 45/7mg/kg BID	45/7
FPV/RTV where FPV was dosed within 40.5-49.5mg/kg	FPV/RTV 45/10 mg/kg BID	45/10
FPV was dosed within 27-33 mg/kg	FPV/RTV 30 mg/kg BID	30
FPV was dosed within 27-33 mg/kg	FPV/RTV 30/7 mg/kg BID	30/7
FPV/RTV where FPV was dosed within 54~66mg/kg	FPV/RTV 60/7 mg/kg BID	60/7
FPV/RTV where FPV was dosed within 54~66mg/kg	FPV/RTV 60/10 mg/kg BID	60/10

7.6. Examination of Subgroups

Some Study Population, Efficacy and Safety summaries may be presented by age group at entry. The age group categories will be 4 weeks to <6months and 6 months to 2 years. Some summaries may also be presented by PI status (PI-experienced or PI-naïve), gender and race.

The following baseline viral load categories will be used in summaries; 400 to-<5,000 copies/mL, 5,000 to-<100,000 copies/mL, 100,000 to-<250,000 copies/mL, 250,000 to-<500,000 copies/mL and ≥500,000 copies/mL. Similarly, the following baseline CD4+ categories will be used; <100 cells/cu mm^3, 100to-<200 cells/cu mm^3, 200 to-<350 cells/cu mm^3, 350 to-<500 cells/cu mm^3 and ≥500 cells/cu mm^3.

PK summaries may be presented by dose and age group at the time of the PK assessment, and for combined age groups. The age group categories will be 4 weeks to– <6 months and 6 months to- <2 years.

7.7. HIV-1 Genotypic and Phenotypic Data

7.7.1. Genotype

Genotypic summaries are based on differences in the plasma HIV-1 sequence from the molecular wild-type strain NL-43. An assessment will be made of the total number of changes across all amino acids within the reverse transcriptase (RT) and protease (PRO) regions, as well as an assessment of specific amino acid changes associated with the development of resistance to antiretrovirals. The specific protease and reverse transcriptase mutations which are associated with the development of resistance as currently defined by the IAS-USA as listed in Table 3. Mutations as defined in the most current version of the IAS-USA guidelines available at the time of data analysis will be used and included in analyses described in this report.

Table 3 Specific Protease and RT mutations associated with the Development of Resistance

NRTI Associated Mutations **M41L, A62V, K65R/E/N, D67N, T69insert, K70R, L74V, V75I, F77L, Y115F, F116Y, Q151M, M184V/I, L210W, T215Y/F, K219Q/E**
Thymidine Analogue Mutations (TAMs) **M41L, D67N, K70R, L210W, T215Y/F, K219Q/E**
NNRTI Analogue Mutations: Major **L100I, K101E/P, K103N, V106A/M, V108I, E138A/G/K/Q, Y181C/I/V, Y188C/L/H, G190A/S, P225H, F227C, M230I/L**
NNRTI Analogue Mutations: Minor **V90I, A98G, K101H, V106I/T, V179D/F/T, G190E, F227L/R, L234I**
Protease Mutations: Major **D30N, V32I, M46I/L, I47V/A, G48V, I50V/L, I54L/M, Q58E, T74P, L76V, V82A/F/T/S/L, N83D, I84V, N88S, L90M**
Protease Mutations: Minor

L10F/I/R/V/C, V11I, G16E, K20M/R/I/T/V, L24I, L33I/F/V, E34Q, M36I/L/V, K43T, F53L/Y, I54V/A/T/S, D60E, I62V, L63P, I64L/M/V, H69K/R, A71V/I/L/T, G73S/A/C/T, V77I, V82I, I85V, N88D, L89I/M/V, I93L/M

Taken from the IAS guideline published in Topics in HIV Medicine: Update of the Drug Resistance Mutations in HIV-1: December 2019 Volume 27 Issue 3 pages 111-121

7.7.2. Phenotypic Data

Phenotypic susceptibility to all licensed antiretroviral drugs will be determined and will be reported as fold change in IC_{50} relative to wild-type control virus (FC). Susceptibilities will be categorised according to FC based on the susceptibility cut-offs published by Monogram as shown in Table 4 or as in the most current cut-offs on the Monogram website at the time of analysis.

Table 4 Fold Change Used to Classify Virus as Sensitive or Resistant: in the Monogram PhenoSense Assay

Drug	Class	Reduced Susceptibility Lower Cut-off[a]	Reduced Susceptibility Upper Cut-off[a]
ABC	NRTI	4.5[a]	6.5
ddI	NRTI	1.3[a]	2.2
3TC	NRTI	3.5[a]	
d4T	NRTI	1.7[a]	
TFV	NRTI	1.4[a]	4
FTC	NRTI	3.5[b]	
ZDV	NRTI	1.9[b]	
DLV	NNRTI	6.2	
EFV	NNRTI	3[b]	
ETV	NNRTI	2.9[a]	10
NVP	NNRTI	4.5[b]	
ATV	PI	2.2	
ATV/r	PI	5.2	
DRV/r	PI	10	90
FPV	PI	2[b]	
FPV/r	PI	4	11
IDV/r	PI	10[a]	

LPV/r	PI	9[a]	55
NFV	PI	3.6 [b]	
RTV	PI	2.5 [b]	
SQV	PI	1.7 [b]	
SQV/r	PI	2.3	12
TPV	PI	2.0[a]	**8**

a. Cut-off determined by clinical evaluation as per Monogram web site, accessed on January 2021 using an advanced proprietary algorithm (version 12)
b. Biologic cut-off as per Monogram web site accessed on January 2021 using an advanced proprietary algorithm (version 12)

8. DATA HANDLING CONVENTIONS

All data manipulations, tabulations, and calculations will be performed using SAS™ Version 9.1.3 on a system of UNIX™ computers.

8.1. Premature Withdrawal and Missing Data

Data recorded at early withdrawal visits will be handled in the same way as scheduled data and will be slotted using the pre-defined visit windows (see Section 9.3).

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 the 'analysis strategies' described. A subject will be considered a completer in the analysis if they remain in the study until Week 48 or until the study it is closed.

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

For proportion based analyses of plasma HIV-1 RNA data the following methods will be employed:

Observed (Obs)

For the EoS analysis, an observed analysis will be performed to evaluate regiment efficacy. For each scheduled assessment time, the rate is defined as follows, where a positive response is defined as plasma HIV-1 RNA response <400 copies/mL (or <50 copies/mL or ≥ 1 $\log_{10}$ copies/mL below baseline):

$$\text{Obs} = \frac{\text{Number of subjects with a positive response where the subject is still receiving study medication}}{\text{Number of subjects in the ITT(E) population with an assessment in the visit Window}}$$

8.1.2. Methods for continuous endpoints based on plasma HIV-1 RNA

For continuous endpoints based on plasma HIV-1 RNA data the following methods will be employed:

Observed

Only subjects who are still receiving investigational product and have data at a visit will be included in the analysis, and no missing values will be imputed. For observed analyses of changes from baseline or actual values, the number of subjects in the analysis at each assessment window may change.

8.1.3. Methods for Other Laboratory Data

For other laboratory data (CD4+ cell counts, haematology and clinical chemistry) the following methods will be employed:

Observed

Only subjects who are still receiving investigational product and have data at a visit will be included in the analysis, and no missing values will be imputed. For observed analyses of actual values, the number of subjects in the analysis at each assessment window may change.

8.1.4. Methods for PK Data

No imputations will be made for missing PK data.

8.1.5. Methods for Missing Dates

In the event that only partial dates are collected in running log pages (e.g. AEs, concurrent medications, background antiretroviral therapy) when full dates are expected and necessary for analyses, the following conventions will apply:

- If the year is missing and cannot be captured, the date will remain missing.
- If start day is missing and cannot be captured, but the month is available, the day will be assigned to the 1st of the month, unless this takes the start date to before treatment start date. In this case the treatment start date will be used. If start day and month is missing and cannot be captured, the day will be assigned to the 1st of January that year, unless this takes the start date to before treatment start date. Again in this case the date of treatment start will be used.
- If stop day is missing and cannot be captured, but the month is available, the day will be assigned to the last day of that month, unless this estimated date comes after the treatment stop date. In this case the treatment stop date is used. If stop day and month is missing and cannot be captured, the day will be assigned to the 31st of December that year, unless this estimated date comes after the treatment stop date. Again in this case the treatment stop date is used.

The 24 week and the 48 week analyses were performed using data from subjects who had not yet completed the study, so a number of subjects had missing treatment stop dates. For this EoS analysis:

- If the treatment stop date is missing, and there is no record of the subject having discontinued then the last assessment date will be used as treatment stop date.

In the event that only partial treatment stop dates are collected when full dates are expected and necessary for analyses, the following conventions will apply:

- Where a month is entered, the imputed treatment stop date is the most relevant date in that month. Where only a year is entered, the imputed treatment stop date is the most relevant date in that year. For example:
- If the investigational product is discontinued due to lost to follow-up, then the last assessment date will be used as treatment stop date, if it falls in the same month/year as the partial date. If it is not in the same month, the last day of the month will be used.
- If the investigational product is discontinued due to virological failure, then the date of the last lab/PCR assessment is used a treatment stop date, if it falls in the same month/year as the partial date. If it is not in the same month, the last day of the month will be used.
- If the investigational product is discontinued and the reason is missing, then the last assessment date will be used as treatment stop date, if it falls in the same month/year as the partial date. If it is not in the same month, the last day of the month will be used.

If an adverse event onset date is completely missing, the adverse event is assumed to have started during treatment and is therefore included in the adverse event summaries.

If the missing date is associated with a scheduled visit (e.g., Week 4) then the missing date will be assigned the target date. The target date will be derived from the subject's treatment start date and the target study day for the scheduled visit as specified in Section 9.3.

For investigational product exposure dates, if the FPV and RTV dates differ, the date for FPV will be used.

8.2. Derived and Transformed Data

Baseline

For Plasma HIV-1 RNA, lymphocyte subsets, genotypic and phenotypic data and all other parameters for which baseline values or changes from baseline are calculated, the baseline value is defined as the value observed at the Day 1 visit or if this value is missing the last value observed before the start of investigational product.

Plasma HIV-1 RNA data

For analyses which use HIV-1 RNA levels as a continuous measure the values will be logged to the base 10.

Quantitative plasma HIV-1 RNA PCR is measured using the Roche Ultrasensitive HIV-1 Monitor Test (Version 1.5, LOD [limit of detection]=50 copies/mL) which can detect HIV-1 RNA values within the range 50-75,000 copies/mL. Samples with HIV-1 RNA results >75,000 copies/mL will be retested using the Roche HIV-1 Monitor Test, version 1.5, standard LOD=400 copies/mL, which can detect HIV-1 RNA values within the range 400-750,000 copies/mL.

In cases where the sample has been retested, the retest value will be used in the analysis. However, in the case that there is only a value reported as <50, <400, >75,000, >750,000 or >7,500,000 copies/mL, the value will be replaced by 49, 399, 75,001, 750,001 or 7,500,001 copies/mL for the purpose of calculating summary statistics, but <50, <400, >75,000, >750,000 or >7,500,000 will be shown in listings.

Due to discontinuation of the Roche Ultrasensitive HIV-1 Monitor Test (Version 1.5, LOD [limit of detection]=50 copies/mL) during the EoS timeframe after the primary endpoint was completed, the assay for determination of HIV-1 RNA viral loads was changed to the Abbott RealTime HIV-1 VL assay. When using the 0.6 mL plasma protocol the linear detection/quantification range is 40 to 10,000,000 copies/mL.

PK Data

No transformations will be made of plasma APV and RTV concentrations.

For FPV and RTV doses where data was captured as ml, these data will be converted to mg/kg as (FPV dose in ml*50(mg/ml))/weight(kg) for FPV and (RTV dose in ml*80mg/ml)/weight(kg) for RTV.

8.2.1. Assessment Windows

For summaries of PK, safety and antiviral activity, data will be assigned to assessments according to the actual visit dates rather than the nominal dates as recorded on the CRF or in the laboratory database. A window around an assessment will include all dates from the midpoints between the target day and that of the previous and proceeding visits and, in general, the nominal target day for week (w) will be (7*w)+1. This visit slotting will be performed according to the time intervals shown in Table 5 with days relative to the date of first dose of FPV/RTV BID investigational product (Day 1).

Table 5 Visit Slotting Intervals

Randomised Period			
Scheduled Visit	**First Day***	**Target Study Day**	**Last Day***
Screening	not applicable	-28	-4
Day 1	-3	1	1
Week 2	2	15	22
Week 4	23	29	43
Week 8	44	57	71
Week 12	72	85	99
Week 16	100	113	141
Week 24	142	169	211
Week 36	212	253	295
Week 48	296	337	379
Week 60	380	422	463
Week 72	464	506	546
Etc.	Etc.	Etc.	Etc.
Follow-up	> (Study Day of last dose + 1)	Study Day of last dose + 28	> (Study Day of last dose + 1)

* Date of assessment – date of first dose + 1

If an assessment window contains more than one value, the value collected closest in time to the target study day will be used for analyses, but all data will be listed. If more than one value is collected the same number of days away from the target study day, the arithmetic mean (geometric mean for HIV-1 RNA data) will be assigned, and for categorical data the worst case scenario will be taken.

The window based method presented above applies to data collected at all scheduled visits (e.g. plasma HIV-1 RNA, other clinical laboratory parameters). Some assessments are not scheduled to be performed at every visit (e.g. health outcomes questionnaires and PK sampling) and for these parameters the windows will be widened if necessary to avoid missing data.

8.3. Values of Clinical Concern

Systems for grading severity of laboratory abnormalities and clinical AEs were included in the protocol. These grades will be utilized in the presentation of the data as described in Section 12.

9. STUDY POPULATION

All tables referred to in this section will be presented on the ITT(E) population, unless otherwise specified. All subjects will be included in listings as appropriate.

9.1. Disposition of Subjects

In general, disposition tables summarizing the disposition of subjects at screen or at baseline for which the data will not have changed since the Week 48 analysis will not be reanalysed for the EoS report; the report will refer back to the results presented in the Week 48 CSR. Subject disposition tables that include additional data collected or representation of the data to account for subjects who continued in the study after Week 48 will be re-analysed for the EoS report.

The following disposition tables will be generated for the EoS report; minor modification to these tables which were included in the Week 48 CSR will be made so that the summaries will describe and differentiate between subjects who continued in the study after Week 48 versus the population who withdrew before or on completion of the Week 48 July 5 2011 cut-off:

- Summary of Investigational Product Status by Age Group at entry for all subjects (h_sp_t001_age)
- Summary of Investigational Product Status by Age Group at entry for subjects who continued after 05July2011 (h_sp_t001_age)
- Summary of Investigational Product Status by Visit (h_sp_t002) including an asterisk for any values obtained after 05July2011
- Summary of End of Study Record for all subjects (h_ds_t001)
- Summary of End of Study Record for subjects who continued after 05July2011 (h_ds_t001)
- Summary of End of Study Record by Visit including an asterisk for any values obtained after 05July2011 (s_ds_t001)

A summary of the number and percentage of subjects who completed the study as well as subjects who withdrew prematurely from the study as recorded in the CRF Study Conclusion page will be produced overall and by visit. A listing of the Study Conclusion page will be produced for the 'All Subjects Enrolled Population'.

9.2. Demographic and Baseline Characteristics

The demographic data tables noted below were generated for the Week 48 report and only demographic analyses which have updates after the 05July2011 data cut-off for the primary analysis will be re-analysed for the EoS report.

Demographic characteristics (gender, age, ethnicity), collected at screening or baseline will be summarised overall and by age group at entry. Date of birth, the screening assessment date, age, gender and ethnicity will be included in the listing of demographic data. Race will be summarised, and a by-subject listing of race will also be produced.

Number and percent of subjects with CDC Classification of HIV Infection Categories N, A, B and C at baseline will be summarised and listed.

HIV risk factor/mode of transmission and current medical conditions at entry will be summarised.

Summary statistics and the distribution of both plasma HIV-1 RNA and CD4+ cell count data (cells/mm^3 and %) at screening and baseline will be presented by age group at entry for subjects who continue after 05July2011.

9.3. Concurrent Medications

For reporting purposes, prior, concomitant and follow-up medications will be defined using the start and stop dates and ongoing fields recorded in the CRF, relative to the first and last dose dates of randomised study medication.

Concurrent medications administered during the study will be coded using the GSK Drug coding dictionary and the following table will be generated:

- Summary of Concomitant Medication Ingredient Combinations for subjects who continue after 05July2011 (h_cm_t003).

A by subject listing of concomitant medications will be produced. The hierarchical relationship between the ATC level 1, ingredient and verbatim text will be listed.

9.4. Prior and Concomitant Antiretroviral Therapy

All prior and concomitant antiretroviral therapy (ART) will be presented including GSK Drug (ATC) classification level 4 (which will provide ART class), ingredient and verbatim text. In the case of multiple ingredients, drugs will be recombined into the combination product if possible (e.g., COMBIVIR, TRIZIVIR).

For reporting purposes, prior, concomitant and follow-up ART medications will be defined using the start and stop dates and ongoing fields recorded in the CRF, relative to the first and last dose dates of randomised study medication. The following tables that summarize concomitant ART or changing NRTIs during the study by PI status in subjects who continued after 05July2011 will be generated:

- Summary of Concomitant Antiretroviral Therapy by PI Status for subjects who continued after 05July2011 (h_cm_t007)
- Summary of Number of Subjects Changing NRTIs During the Study by PI Status for subjects who continued after 05July2011 (s_cm_t004).

Prior and concomitant ART will be listed. Summary tables were generated for the 48 week report and therefore only tables that deal with concomitant (or follow-up) antiretroviral therapy after 05July2011 will be updated for the EoS report.

Listings will be generated for subject disposition as follows though the end of study and will differentiate between subjects who continued in the study after 05July2011 (week 48 data cut-off date) with the addition of an asterisk vs those who did not:

- Listing of Investigational Product Discontinuation and reason for discontinuation(h_sp_l001)
- Listing of End of Study Record (h_ds_l002)

- Listing of Demographic Characteristics (h_dm_l001)
- Listing of Race (h_dm_l002)
- Listing of Concomitant Medications (h_cm_l001)
- Listing of Concomitant Antiretroviral Therapy (h_cm_l004)
- Listing of Study Populations (h_pn_1001)
- Listing of Concomitant medication Relationship between ATC Level 1, Ingredient and Verbatim Text (h_cm_1002)
- Listing of Prior Antiretroviral Therapy (h_cm_1003)
- Listing of Important Protocol Deviations

10. ANTIVIRAL RESPONSE ANALYSES

All antiviral response analyses will be performed on the ITT(E) Population, unless otherwise stated. All subjects will be included in listings as appropriate.

10.1. Protocol Deviations

All violations of inclusion/exclusion criteria will be listed.

10.2. Proportion of Subjects with Plasma HIV-1 RNA levels Below 400 copies/mL at each Visit

For the EoS analysis, the proportion of subjects with plasma HIV-1 RNA level below 400 copies/mL will be presented for each visit using the Observed analysis strategy.

10.3. Proportion of Subjects with Plasma HIV-1 RNA levels Below 50 copies/mL at each Visit

For the EoS analysis, the proportion of subjects with plasma HIV-1 RNA level below 50 copies/mL will be presented for each visit. This analysis will be performed using the Observed analysis strategy (see Section 8.1.1).

In addition to the above, the viral load data will be listed by subject and by visit.

10.4. Measured values and change from baseline in plasma HIV-1 RNA $\log_{10}$ copies/mL

The actual values and changes from baseline in plasma HIV-1 RNA $\log_{10}$ copies/mL will be summarised and will be presented for each visit. This analysis will be performed using the Observed analysis strategy (see Section 8.1.1) and the data will be listed**.** The actual values will also be presented by age group at entry, gender and race.

10.5. Measured values and change from baseline in CD4+ cell counts

The actual values and changes from baseline in CD4+ cell count (cells/mm^3 and %) will be summarised by age group at entry and presented by visit for the Observed analysis strategy (see Section 8.1.1) and the data will also be listed.

10.6. HIV Associated Conditions

All data collected on HIV associated conditions will be listed.

A summary of all treatment emergent HIV associated conditions including those which are a recurrence of a previous condition will be presented for subjects with data after the 05July2011 cut-off. Similar summaries will be presented which exclude those HIV associated conditions which are a recurrence of a previous condition.

10.7. HIV Disease Progression

Proportions of subjects experiencing clinical disease progression or death after the 05July2011 data cut-off for the Week 48 analysis will be presented.

Clinical disease progression is defined as the progression from baseline HIV disease status as follows:

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

11. SAFETY ANALYSES

All safety tables are based on the Safety Population. All subjects will be included in listings as appropriate.

11.1. Extent of Exposure

For the EoS population continuing treatment following the week 48 report cut-off date (05July2011), the date a subject discontinued together with details of the reason for those subjects who discontinued will be listed (as collected on the Investigation Product Record and Investigation Product Discontinuation Record pages).

11.2. Adverse Events

Adverse events will be coded using the 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 lower level term, preferred term and system organ class. A listing of the relationship of preferred term to lower level terms and investigator text will be presented ordered by system organ class.

The following sets of treatment emergent adverse events (i.e. those with onset date on or after initiation of investigational product, and up to the day of the last dose of investigational product) will be tabulated. A cumulative summary of treatment emergent adverse events in all subjects will be generated and a summary of treatment emergent AEs for subjects who continued after 05July2011 (week 48 data cut-off date) through EoS will be generated. In order to account for any duplication of the same AE reported in both the week 48 report and in the EoS population, a comparison will be performed for AEs in the subjects remaining on treatment after 05July2011 (as there were 25 subjects in the study on July 5, 2011, it is estimated that this n=25) and any duplication will be noted in the EoS report. For AEs captured more than once, the most severe intensity will be included in summaries, and all events will be included in the following listings:

- Table 3.01 Summary of All Treatment Emergent Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (h_ae_t001_all)
- Table 3.02 Summary of All Treatment Emergent Adverse Events by System Organ Class for all study participants (h_ae_t001_all)
- Table 3.11 Summary of All Treatment Emergent Adverse Events by System Organ Class and Maximum Toxicity/Intensity for subjects who remained on treatment after 05July2011 (h_ae_t004_all)
- Table 3.12 Summary of All Treatment Emergent Adverse Events by System Organ Class and Maximum Toxicity/Intensity for all study participants (h_ae_t004_all)
- Table 3.21 Summary of All Treatment Emergent Adverse Events by System Organ Class by Age Group at Entry for subjects who remained on treatment after 05July2011 (h_ae_t002_age)
- Table 3.22 Summary of All Treatment Emergent Adverse Events by System Organ Class by Age Group at Entry for all study participants (h_ae_t002_age)
- Table 3.31 Summary of All Treatment Emergent Adverse Events by Frequency for subjects who remained on treatment after 05July2011 (h_ae_t003)
- Table 3.32 Summary of All Treatment Emergent Adverse Events by Frequency for all study participants (h_ae_t003)
- Table 3.41 Summary of Treatment Emergent Grade 2-4 Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (h_ae_t001_24)

- Table 3.42 Summary of Treatment Emergent Grade 2-4 Adverse Events by System Organ Class for all study participants (h_ae_t001_24)
- Table 3.51 Summary of Treatment Emergent Grade 2-4 Adverse Events by Frequency for subjects who remained on treatment after 05July2011 (h_ae_t003_24)
- Table 3.52 Summary of Treatment Emergent Grade 2-4 Adverse Events by Frequency for all study participants (h_ae_t003_24)
- Table 3.61 Summary of Treatment Emergent Grade 2-4 Adverse Events by System Organ Class and Age Group at Entry for subjects who remained on treatment after 05July2011 (h_ae_t001_24_age)
- Table 3.62 Summary of Treatment Emergent Grade 2-4 Adverse Events by System Organ Class and Age Group at Entry for all study participants (h_ae_t001_24_age)
- Table 3.71 Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (h_ae_t001_dr)
- Table 3.72 Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class for all study participants (h_ae_t001_dr)
- Table 3.81 Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class and Maximum Toxicity for subjects who remained on treatment after 05July2011 (h_ae_t004_dr)
- Table 3.82 Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class and Maximum Toxicity for all study participants (h_ae_t004_dr)
- Table 3.91 Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class and Age Group at Entry for subjects who remained on treatment after 05July2011 (h_ae_t004_dr_age)
- Table 3.92 Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class and Age Group at Entry for all study participants (h_ae_t004_dr_age)
- Table 3.101 Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (h_ae_t001_dr_24)
- Table 3.102 Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by System Organ Class for all study participants (h_ae_t001_dr_24)
- Table 3.111 Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by Frequency for subjects who remained on treatment after 05July2011 (h_ae_t003_dr_24)
- Table 3.112 Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by Frequency for all study participants (h_ae_t003_dr_24)

- Table 3.121 Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by System Organ Class and Age Group at Entry for subjects who remained on treatment after 05July2011 (h_ae_t001_dr_24_age)
- Table 3.122 Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by System Organ Class and Age Group at Entry for all study participants (h_ae_t001_dr_24_age)
- Table 3.131 Summary of Treatment Emergent Grade 3/4 Adverse Events by Frequency for subjects who remained on treatment after 05July2011 (h_ae_t001_34)
- Table 3.132 Summary of Treatment Emergent Grade 3/4 Adverse Events by Frequency for all study participants (h_ae_t001_34)
- Table 3.141 Summary of Treatment Emergent Serious Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (h_ae_t001_ser)
- Table 3.142 Summary of Treatment Emergent Serious Adverse Events by System Organ Class for all study participants (h_ae_t001_ser)
- Table 3.151 Summary of Treatment Emergent Serious Adverse Events by System Organ Class and Age Group at Entry for subjects who remained on treatment after 05July2011 (h_ae_t001_ser_age)
- Table 3.152 Summary of Treatment Emergent Serious Adverse Events by System Organ Class and Age Group at Entry for all study participants (h_ae_t001_ser_age)
- Table 3.161 Summary of Drug Related Treatment Emergent Serious Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (h_ae_t001_dr_ser)
- Table 3.162 Summary of Drug Related Treatment Emergent Serious Adverse Events by System Organ Class for all study participants (h_ae_t001_dr_ser)
- Table 3.171 Summary of Treatment Emergent Adverse Events Leading to Permanent Discontinuation of Chronic FPV for subjects who remained on treatment after 05July2011 (h_ae_t001_disc)
- Table 3.172 Summary of Treatment Emergent Adverse Events Leading to Permanent Discontinuation of Chronic FPV for all study participants (h_ae_t001_disc)
- Table 3.181 Summary of Treatment Emergent Adverse Events Leading to Withdrawal from the Study for subjects who remained on treatment after 05July2011 (h_ae_t001_wdw)
- Table 3.182 Summary of Treatment Emergent Adverse Events Leading to Withdrawal from the Study for all study participants (h_ae_t001_wdw)
- Table 3.191 Summary of All Episodes of Selected Drug Related Treatment Emergent AEs by Days to Onset, Duration, Status, Intensity and Action Taken for subjects who remained on treatment after 05July2011 (s_ae_t003)

- Table 3.192 Summary of All Episodes of Selected Drug Related Treatment Emergent AEs by Days to Onset, Duration, Status, Intensity and Action Taken for all study participants (s_ae_t003)
- Table 3.201 Summary of Treatment Emergent Rash Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (t_ae_t002_rash)
- Table 3.202 Summary of Treatment Emergent Rash Adverse Events by System Organ Class for all study participants (t_ae_t002_rash)
- Table 3.211 Summary of Clinical Chemistry by Visit – Parameters of Special Interest by Age Group at Entry for subjects who remained on treatment after 05July2011 (h_lb_t001_chem_sp_age)
- Table 3.212 Summary of Clinical Chemistry by Visit – Parameters of Special Interest by Age Group at Entry for all study participants (h_lb_t001_chem_sp_age)
- Table 3.221 Summary of Clinical Chemistry by Visit – All Other Parameters for subjects who remained on treatment after 05July2011 (h_lb_t001_chem_oth)
- Table 3.222 Summary of Clinical Chemistry by Visit – All Other Parameters for all study participants (h_lb_t001_chem_oth)
- Table 3.231 Summary of Haematology by Visit for subjects who remained on treatment after 05July2011 (h_lb_t001_hem)
- Table 3.232 Summary of Haematology by Visit for all study participants (h_lb_t001_hem)
- Table 3.241 Summary of Clinical Chemistry Toxicities – Total for subjects who remained on treatment after 05July2011 (s_lb_t003_chem)
- Table 3.242 Summary of Clinical Chemistry Toxicities – Total for all study participants (s_lb_t003_chem)
- Table 3.251 Summary of Clinical Chemistry Toxicities – Parameters of Special Interest for subjects who remained on treatment after 05July2011 (s_lb_t003_chem_sp)
- Table 3.252 Summary of Clinical Chemistry Toxicities – Parameters of Special Interest for all study participants (s_lb_t003_chem_sp)
- Table 3.261 Summary of Clinical Chemistry Toxicities – All Other Parameters for subjects who remained on treatment after 05July2011 (s_lb_t003_chem_othf)
- Table 3.262 Summary of Clinical Chemistry Toxicities – All Other Parameters for all study participants (s_lb_t003_chem_othf)
- Table 3.271 Summary of Haematology Toxicities for subjects who remained on treatment after 05July2011 (s_lb_t003_hem)
- Table 3.272 Summary of Haematology Toxicities for all study participants (s_lb_t003_hem)

- Table 3.281 Summary of Vital Signs Data by Visit for subjects who remained on treatment after 05July2011 (h_vs_t001)
- Table 3.282 Summary of Vital Signs Data by Visit for all study participants (h_vs_t001)
- Table 3.291 Summary of Abacavir Hypersensitivity Record for subjects who remained on treatment after 05July2011 (h_abc_t001)
- Table 3.292 Summary of Abacavir Hypersensitivity Record for all study participants (h_abc_t001)
- Table 3.301 Summary of Common (≥5% Frequency) Non Serious Treatment Emergent Adverse Events by Overall Frequency for subjects who continued treatment after 05July2011 (h_ae_fdaaa)
- Table 3.302 Summary of Common (≥5% Frequency) Non Serious Treatment Emergent Adverse Events by Overall Frequency for all study participants (h_ae_fdaaa)
- Table 3.310 Summary of COVID-19 Assessment for Subjects with COVID-19 Adverse Events(PAN1)
- Table 3.320 Summary of COVID-19 Symptoms for Subjects with COVID-19 Adverse Events(PAN3)

These adverse event incidence rates will be calculated using the total number of subjects in the Safety Population as the denominator.

A summary of common (≥5%) non-serious adverse events will be provided for use in the FDAAA template. Serious adverse events will be excluded from the summary and the denominator will be the number of subjects reported at least one of the most common (≥5%) non-serious adverse events.

The following safety figures will be included:

- Figure displaying the time to onset, duration, severity and outcome of the first occurrence of the selected drug-related AEs of special interest (above) will be presented.
- Individual patient profile plots of LFTs for Subjects who Experience a Grade 3 or 4 LFT Toxicity
- Individual patient profile plots of Neutrophils, Lymphocytes and White Blood Cells for Subjects who Experience a Grade 3 or 4 Neutrophil Toxicity

The following listings will also be listed with the addition of an asterisk to indicate that the adverse event occurred after 05July2011:

- Listing of Exposure Data
- Listing of all adverse events
- Listing of fatal adverse events
- Listing of non-fatal serious adverse events
- Listing of subject numbers for individual adverse events

- Listing of clinical chemistry data for subjects with laboratory abnormalities
- Listing of haematology data for subjects with laboratory abnormalities
- Listing of subjects who discontinued

  Listing of adverse events leading to permanent discontinuation of investigational product
- Listing of adverse events leading to withdrawal from the study Listing of all adverse events for subjects who experienced any rash
- Listing of Relationship of MedDRA Preferred Terms to Lower Level Terms and Adverse Event Investigator Text
- Listing of Clinical Chemistry Data
- Listing of Haematology Data
- Listing of Laboratory Data from Local Labs
- Listing of Vital Signs Data
- Listing of Clinical Chemistry Laboratory Data for Subjects with Laboratory Abnormalities of Potential Clinical Concern(LB5)
- Listing of Haematology Laboratory Data for Subjects with Laboratory Abnormalities of Potential Clinical Concern(LB5)
- Listing of the relationship of adverse event system organ classes, preferred terms and verbatim text

11.3. Deaths and Serious Adverse Events

Deaths and serious adverse events will be reported as detailed in the Section 11.2.

11.4. 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 will be reported as detailed in the section 11.2.

Any subjects experiencing an Abacavir Hypersensitivity Reaction (ABC HSR) were required to complete the ABC HSR Record in the CRF. The number of subjects experiencing an ABC HSR will be summarized and all data will be listed.

11.5. Clinical Laboratory Evaluations

Laboratory data are given in standard units by the central laboratory (see protocol for a list), and only these values will be presented in summaries and listings. Non-numeric values that contain an embedded number (e.g. '>100', '<1.9') will be interpreted as

having a value equal to the numeric portion for data analysis plus/minus a meaningful quantity, but presented ‘as is’ in the listings.

Individual haematology, clinical chemistry and lipid data are flagged as above (H) or below (L) the appropriate normal range of the central laboratory and with respect to toxicity grades according to the toxicity scales. Some flags may be calculated during the analysis using the ranges provided in the protocol. These flags and toxicity grades will be included in the listings of clinical chemistry and haematology data, which will be by treatment, investigator number, subject number and visit.

All parameters e will be presented using summary statistics by visit. Separate summaries will be displayed for clinical chemistry parameters of special interest (ALT, AST, triglycerides, HDL, LDL, total cholesterol, lipase, hyperglycaemia and hypoglycaemia), clinical chemistry for all other parameters and haematology. Clinical chemistry data and haematology data will be listed. The summary of actual values for the clinical chemistry parameters of special interest will be presented by age group at entry. For the EoS report, summaries will distinguish between data that was reported after 05July2011 (Week 48 data cut-off) through EoS versus results reported cumulatively throughout the study.

Summaries of all treatment emergent clinical chemistry and hematology toxicities will be produced. A summary of clinical chemistry toxicities will also be produced separately for the parameters of special interest and all other parameters. A graded toxicity is considered treatment emergent if it develops or increases post baseline in intensity (and prior to last dose of investigational product). Listings of subjects reporting at least one *Grade 3 or 4* laboratory abnormality of potential clinical concern will be presented.

Individual patient profile plots for liver function tests (LFTs) will be produced for all subjects who experience a Grade 3 or 4 toxicity in at least of the LFTs during the study; LFTs are AST, ALT, Bilirubin and Alkaline Phosphatase. Individual patient profile plots for neutrophils, lymphocytes and white blood cells will be produced for all subjects who experience a Grade 3 or 4 neutrophil toxicity.

Data from local laboratories will be listed separately from the central laboratory data and will not be included in the summaries unless there is significant missing data in which case local and central laboratory data may be combined.

11.6. Other Safety Measures

Summary statistics of actual values in blood pressure, heart rate, height, and weight and head circumference during the study will be presented by visit and the data listed.

12. CLINICAL PHARMACOLOGY DATA ANALYSES

The EoS report will not contain a formal pharmacokinetic analysis. Generation of summary statistics and listings for the remaining pharmacokinetic samples will be the responsibility of stats and programming (SMP)

12.1. Bioanalysis

Drug analysis was the responsibility of the Department of Worldwide Bioanalysis, Drug Metabolism and Pharmacokinetics. Plasma PK samples were analysed for APV, FPV, and RTV concentrations using a validated analytical method.

12.2. Pharmacokinetic Analyses

The previous Week 48 PK analysis of the plasma APV and RTV concentration-time data using non-compartmental methods was conducted by the GSK Department of CPMS using Winnonlin™ Version 4.1 or higher (Pharsight Corporation, Mountain View, CA, USA) for the Week 48 CSR. Actual plasma PK sample collection times were used in the PK analysis.

For the APV20002 study, primary analysis of PK data from subjects was completed at week 48 and 05July2011 was the cut off point for data used in the original report. A small number of additional PK samples (<10% of the total PK data) was collected and approved after the 05July2011 cut-off date up to a timepoint of September 26, 2011.

Since 2012, weight based dosing has been implemented for FPV OS based on the Week 48 PK analysis in countries where this FPV OS is marketed and no new safety concerns have arisen regarding the use of the dosage recommended in the 48 week CSR. Given that the FPV OS paediatric dosing regimen for this age and weight group has been available since 2012, it is unlikely that the reanalysis of all PK data to include this small number of additional PK samples would increase our understanding or change current FPV OS dosing recommendations. Therefore, two tables of descriptive statistics (see Section 16.1) summarizing the PK data will be produced for the additional PK samples collected between July 6 and Sept 26, 2011. The tables and listings will include the following:

- 10.1 , Summary of APV concentrations (mean and standard deviation, median and 95% percentile)
- 10.2 , Summary of RTV concentrations (mean and standard deviation, median and 95% percentile)
- 10.3 , Listing of Plasma APV Concentration Data (mg/mL) (by Subject and Visit)
- 10.4 , Listing of Plasma RTV Concentration Data (mg/mL) (by Subject and Visit)

13. VIRAL GENOTYPING/PHENOTYPING

Plasma samples for HIV viral resistance testing (PhenosenseGT**,** Monogram Biosciences Inc) were collected from all subjects at baseline (Day 1) for evaluation of baseline reverse transcriptase (RT) and protease (PR) mutations, and phenotypic resistance.

A specific comprehensive definition for virologic failure was not included in the original APV20002 protocol. In subsequent protocol amendments, to be consistent with the then current standard practice, for the 24 Week analysis, virologic failure was defined as

failure to achieve a plasma HIV-RNA by Week 24 or confirmed HIV-RNA rebound to ≥400 copies/mL after achieving a plasma HIV-RNA of <400 copies/mL. The Week 48 analysis included subjects defined as virological failures in the Week 24 interim analysis along with subjects who had a confirmed HIV-RNA rebound to ≥400 copies/mL after achieving a plasma HIV-RNA of <400 copies/mL between Week 24 and Week 48. If a subject had a single viral load rebound ≥400 copies/mL at Week 48 and it was their last available visit at the time of the 05July2011 data cut, virological failure could not be confirmed, and those subjects were not included in the Virological Failure Population for the 48 week analysis.

For the EoS analysis, the same definition of virologic failure (confirmed HIV-RNA rebound to ≥400 copies/mL after achieving a plasma HIV-RNA of <400 copies/mL) will be applied for subjects who continued in the study after Week 48. Given the limited sample material available for analysis any result obtained up to 12 weeks after the virologic failure analysis point will be used in the analysis (if there are 2 results within this time window, the closest to the initial virologic failure timepoint will be used).

A summary of the number of subjects who have provided genotypic and phenotypic data from their HIV-1 isolates will be presented for both the Baseline Virology and Virological Failure Populations. However, any genotypic and phenotypic data obtained for subjects who are unconfirmed virologic failures will be included in the listings along with data from subjects who met confirmed virologic failure, but data from subjects who are unconfirmed virologic failures will not be further analyzed.

Mutations included in the virology analyses are those in the RT and PRO regions of the HIV genome which are NRTI, NNRTI, or PI resistance-associated amino acid substitutions (see Section 8.4).

Subjects with confirmed virological failure after Week 48 will be summarized separately from any summary of subjects who met the criteria for confirmed virologic failure by Week 48 in summary tables generated for the EoS analysis. To better describe the virologic failures that occurred after the Week 48 analysis data cut-off (05July2011) compared to those that occurred by Week 48, the tables describing the two populations will include the following:

- Table 11.01 A Summary of Subject Accountability by Age Group: Populations describing the total virology population, the baseline virology population, the total confirmed virologic failure population and the confirmed virologic failure population after Week 48 to EoS
- Table 11.02 A Summary of Subject Accountability Genotypic Data Available – baseline virology population summarizing the number of subjects with HIV RT and PRO mutation data at baseline, the number of subjects with baseline data; all subjects with virologic failure timepoint data, all subjects with matched baseline and virologic failure timepoint samples all subjects with virologic failure (after week 48 through EoS) data and subjects with virologic failure (after week 48 through EoS) with matched baseline and failure timepoint data
- Table 11.03 A Summary of Subject Accountability Genotypic Data Available – Virological Failure Population summarizing the number of subjects with HIV RT

and protease (PR) mutation data at virologic failure for the confirmed virologic failure population; including the total numbers of subjects with confirmed virologic failure, the number of these subjects with baseline data, all subjects with matched baseline and virologic failure timepoint data; those subjects with virologic failure (after week 48 through EoS) and those subjects with virologic failure (after week 48 through EoS) with matched baseline and failure timepoint sample data

- Table 11.04 A Summary of Subject Accountability Phenotypic Data Available – baseline virology population summarizing the number of subjects with phenotypic data (for each drug class NRTI, NNRTI and PI) at baseline, for all subjects with virologic failure data; all subjects with matched baseline and virologic failure timepoint data and those with data at both baseline and virologic failure (after week 48 through EoS) and those subjects with virologic failure (after week 48 through EoS) with matched baseline and failure sample data
- Table 11.05 Summary of Subject Accountability Phenotypic Data Available – Virological Failure Population summarizing the number of subjects with phenotypic drug resistance data for each drug class NRTI, NNRTI and PI for the confirmed virologic failure population through and the confirmed virologic failure population after Week 48 to EoS. including the total numbers of subjects with confirmed virologic failure, the number of these subjects with baseline data, all subjects with matched baseline and virologic failure timepoint data; those subjects with virologic failure (after week 48 through EoS) and those subjects with virologic failure (after week 48 through EoS) with matched baseline and failure timepoint sample data
- Table 11.11 Summary of End of Study Record - Virological Failure Population for two groups- the confirmed virologic failure population for all subjects with confirmed virologic failures
- Table 11.12 Summary of End of Study Record - Virological Failure Population for the the confirmed virologic failure population after Week 48 to EoS
- Table 11.21 Summary of Baseline Characteristics - Virological Failure Population for all subjects with confirmed virologic failure
- Table 11.22 Summary of Baseline Characteristics - Virological Failure Population for the confirmed virologic failure population after Week 48 to EoS

NRTI, NNRTI and PI resistance associated genotypic mutations in the HIV RT and PR regions will be summarized for both the Baseline Virology and Virological Failure populations by ART/PI status (ART naïve vs. ART experienced with ART experienced subjects further subdivided into PI naïve vs PI experienced. These summary tables will differentiate between confirmed virologic failures that occurred by Week 48 versus confirmed virologic failures which occurred after Week 48. Baseline is defined as the Day 1 result unless this is missing in which case the screening result will be used. These summary tables will include:

- Table 11.31 Summary of PR and RT Genotypic Mutations at Failure Timepoint by ART/PI Status – Virological Failure Population for the confirmed virologic failure population after Week 48 to EoS
- Table 11.32-Summary of PR and RT Genotypic Mutations at Failure Timepoint by ART/PI Status – Virological Failure Population for all Virologic Failure

- Table 11.41 Summary of Baseline RT and PR Mutations Associated with Each Drug Class at the virologic failure timepoint for confirmed virologic failures after Week 48 to EoS – Virological Failure Population
- Table 11.42 Summary of Baseline RT and PR Mutations Associated with Each Drug Class at the virologic failure timepoint for all Virologic failures – Virological Failure Population
- Table 11.50 Summary of RT and PR Mutations by Subject and Visit – Virological Failure Population. Footnotes to be included * Indicates that the sample was used as part of a virological failure paired sample; # Indicates a treatment emergent mutation and ^^ after the Subject ID indicates the subject met confirmed virologic failure after Week 48 through EoS
- Table 11.61 Summary of Treatment Emergent PRO and RT Genotypic Mutations by ART/PI Status – Virological Failure Population after Week 48 to EoS. Treatment emergent mutations are defined as mutations detected post baseline at the virologic failure timepoint that were not present in the baseline sample.
- Table 11.62 Summary of Treatment Emergent PRO and RT Genotypic Mutations by ART/PI Status – Virological Failure Population (s_geno_te)
- Table 11.71 Summary of Treatment Emergent RT and PR Mutations at Failure Timepoint Associated with Each Drug Class – Virological Failure Population after Week 48 through EOS
- Table 11.72 Summary of Treatment Emergent RT and PR Mutations at Failure Timepoint Associated with Each Drug Class – Entire Virological Failure Population
- Table 11.81 Summary of Genotypic Resistance defined by IAS-USA guidelines at Baseline and Failure Timepoint by Treatment, ART/PI Status and Subject – Virological Failure Population (s_geno_IAS pi_fail). Note: ^^ *after the Subject ID indicates the subject met confirmed virologic failure after Week 48 through EoS*
- Table 11.82 Summary of Genotypic Resistance defined by IAS-USA guidelines at Baseline and Failure Timepoint by Treatment, Age Group at Entry Status and Subject – Virological Failure Population (s_geno_IAS_age_fail) *Note: ^^ after the Subject ID indicates the subject met confirmed virologic failure after Week 48 through EoS*

For the Phenotypic resistance data, a table summarizing phenotypic Fold Resistance by Subject and Visit for the Virological Failure Population for each drug tested in the Monogram assay will be generated. One table will summarize fold resistance by subject and visit for those subjects who met virologic failure criteria after Week 48 through EoS, while the second table will summarize fold resistance by subject and visit from all subjects who met confirmed Virologic Failure criteria throughout the entire study. visit distinguish between subjects who became confirmed virologic failures by Week 48 vs those that occurred after Week 48.

- Table 11.91 Summary of Fold Resistance by Subject and Visit - Virological Failure Population after Week 48 through EoS (s_fr_subj_fail) Footnote to be included * Indicates that the sample was used as part of a virological failure paired sample

- Table 11.92 Summary of Fold Resistance by Subject and Visit - Entire Virological Failure Population (s_fr_subj_fail) Footnote to be included * Indicates that the sample was used as part of a virological failure paired sample

Treatment Emergent reduced susceptibility (resistance) at the Failure Timepoint by ART/PI Status – Virological Failure Timepoint will be generated that distinguishes between confirmed virologic failures that occurred by Week 48 vs those that occurred after Week 48

- Table 11.101 Summary of Treatment Emergent Susceptibility at Failure Timepoint by ART/PI Status – Virological Failure Timepoint Virologic Failure Population after Week 48 through EoS
- Table 11.102 Summary of Treatment Emergent Susceptibility at Failure Timepoint by ART/PI Status – Virological Failure Timepoint -Entire Virologic Failure Population

The total Virology Population will be listed. All genotypic data collected will be included in separate listings of RT and PR mutations. All phenotypic data will be listed. The phenotypic data will also be listed by the on-therapy background drugs. Clade assignment and replicative capacity data will also be listed. These listings will also include the Subject ID, sample date and actual relative time, as appropriate. All listings will be presented as bulleted below:

- Listing of Subject Accountability: Populations
- Listing of Reverse Transcriptase Mutations)
- Listing of Protease Mutations
- Listing of Phenotypic Data
- Summary of Phenotypic Data for On-Therapy drugs by Subject
- Listing of Clade assignment
- Listing of Replicative Capacity Data

14. COVID - 19 ANALYSIS

This study was started in 2012 and is being continued during the outbreak of the ongoing COVID -19 pandemic. The information regarding the number of subjects affected by COVID-19 and its symptoms will be reported according to GSK core standards. Any visits impacted due to the pandemic outbreak will be reported. Protocol deviations or adverse events related to COVID-19 if any, will also be reported according to GSK core standards.

15. REFERENCES

GlaxoSmithKline Document Number GD2001/00007/00 Study ID: APV20002. A 48 Week Phase II, Open-label, 2-cohort, Multicentre Study to Evaluate the Pharmacokinetics, Safety, Tolerability and Antiviral Activity of GW433908 and GW433908/RTV When Administered to HIV-1 Infected Protease Inhibitor (PI) Naïve and PI-Experienced Pediatric Subjects aged 6 weeks to <2 years. Effective date:20 Sept-2002.

GlaxoSmithKline Document Number GD2001/00007/12. Protocol Amendment 12. APV20002: A 48 Week Phase II, Open-label, 2-cohort, Multicenter Study to Evaluate the Pharmacokinetics, Safety, Tolerability and Antiviral Activity of GW433908 and GW433908/RTV When Administered to HIV-1 Infected Protease Inhibitor (PI) Naïve and PI-Experienced Paediatric Subjects aged 4 weeks to <2 years. Effective date:30 Nov-2019.

GlaxoSmithKline Document Number RM2006/00360/00. A 48 Week Phase II, Open-label, 2-cohort, Multicenter Study to Evaluate the Pharmacokinetics, Safety, Tolerability and Antiviral Activity of GW433908 and GW433908/RTV When Administered to HIV-1 Infected Protease Inhibitor (PI) Naïve and PI-Experienced Paediatric Subjects aged 4 weeks to <2 years. Effective date:20-SEP-2006.

GlaxoSmithKline Document Number 2010N107734_00. A 48 Week Phase II, Open-label, 2-cohort, Multicenter Study to Evaluate the Pharmacokinetics, Safety, Tolerability and Antiviral Activity of GW433908 and GW433908/RTV When Administered to HIV-1 Infected Protease Inhibitor (PI) Naïve and PI-Experienced Paediatric Subjects aged 4 weeks to <2 years. Effective date:08-JUN-2011.

GlaxoSmithKline Document Number 2010N107734_01. A 48 Week Phase II, Open-label, 2-cohort, Multicenter Study to Evaluate the Pharmacokinetics, Safety, Tolerability and Antiviral Activity of GW433908 and GW433908/RTV When Administered to HIV-1 Infected Protease Inhibitor (PI) Naïve and PI-Experienced Paediatric Subjects aged 4 weeks to <2 years. Effective date:30-JUN-2011.

GlaxoSmithKline Document Number 2011N127273_00_01. A 48 Week Phase II, Open-label, 2-cohort, Multicenter Study to Evaluate the Pharmacokinetics, Safety, Tolerability and Antiviral Activity of GW433908 and GW433908/RTV When Administered to HIV-1 Infected Protease Inhibitor (PI) Naïve and PI-Experienced Paediatric Subjects aged 4 weeks to <2 years. Effective date:24-APR-2012.

16. ATTACHMENTS

16.1. Table of Contents for Data Display Specifications

Study Population and Baseline Characteristic Tables

Table	Title
1.01	Summary of Investigational Product Status by Age Group at entry (h_sp_t001_age) for all subjects
1.02	Summary of Investigational Product Status by Age Group at entry (h_sp_t001_age) for subjects who continued after 05July2011
1.03	Summary of Investigational Product Status by Visit (h_sp_t002) with asterisk for any subject after 05July2011
1.04	Summary of End of Study Record (h_ds_t001) for all subjects
1.05	Summary of End of Study Record (h_ds_t001) for subjects included after 05jul2011
1.06	Summary of End of Study Record by Visit (s_ds_t001) with asterisk for values obtained after 05July2011
1.07	Distribution of Quantitative Plasma HIV-1 RNA Results at Screening and Baseline by Age Group at entry for subjects who continued after 05July2011(s_vl_t001_age)
1.08	Distribution of CD4+ Cell Count (cells/cu mm) Results at Screening and Baseline by Age Group at entry for subjects who continued after 05July2011(s_cd_t001_ct_age)
1.09	Summary of Concomitant Medication Ingredient Combinations for subjects who continued after 05july2011 (h_cm_t003)
1.11	Summary of Concomitant Antiretroviral Therapy by PI Status for subjects who continued after 05july2011 (h_cm_t007)
1.12	Summary of Number of Subjects Changing NRTIs During the Study by PI Status for subjects who continued after 05July2011 (s_cm_t004)

Study Population and Baseline Characteristics ICH Listings (Note: subjects who continued after 05July2011 will be denoted with an asterisk)

Listing	Title
1.	Listing of Investigational Product Discontinuation *(h_sp_l001)*
2.	Listing of End of Study Record *(h_ds_l002)*
3.	Listing of Demographic Characteristics (h_dm_l001)
4.	Listing of Race (h_dm_l002)
5.	Listing of Concomitant Medications (h_cm_l001)
6.	Listing of Concomitant Antiretroviral Therapy *(h_cm_l004)*

Study Population and Baseline Characteristic Other Listings (Note: subjects who continued after 05July2011 will be denoted with an asterisk)

Listing	Title
1	Listing of Study Populations *(h_pn_l001)*
2	Listing of Concomitant Medication Relationship between ATC Level 1, Ingredient and Verbatim Text *(h_cm_l002)*
3	Listing of Prior Antiretroviral Therapy *(h_cm_l003)*
4	Listing of Important Protocol Deviations

Antiviral Response Tables

Table	Title
2.01	Proportion of Subjects with Quantitative Plasma HIV-1 RNA <400 copies/ml by Visit – Observed (*h_prp_t001_400_obs)*
2.02	Proportion of Subjects with Quantitative Plasma HIV-1 RNA <50 copies/ml by Visit – Observed (h_prp_t001_50_obs)
2.03	Proportion of Subjects with Quantitative Plasma HIV-1 RNA at Least 1.0log10 copies/ml below Baseline by Visit – Observed (h_prp_t001_1log_obs)
2.04	Summary of Quantitative Plasma HIV-1 RNA Results by Visit (log10 copies/ml) – Observed (h_vl_t002)
2.05	Summary of Quantitative Plasma HIV-1 RNA Results by Visit and Age Group (log10 copies/ml) – Observed (h_vl_t002_age)
2.06	Summary of Quantitative Plasma HIV-1 RNA Results by Visit and Gender (log10 copies/ml) – Observed (h_vl_t002_sex)
2.07	Summary of Quantitative Plasma HIV-1 RNA Results by Visit and Race (log10 copies/ml) – Observed (h_vl_t002_race)
2.08	Summary of Quantitative Plasma HIV-1 RNA Changes from Baseline by Visit (log10 copies/ml) – Observed (h_vl_t002_chg)
2.09	Summary of CD4+ Cell Count (cells/cu mm) – Results by Visit and Age Group Observed (h_cd_t002_4_ct_age)
2.10	Summary of HIV Associated Conditions Including Recurrences for Children (h_cdc_t001_inc_child)
2.11	Summary of HIV Associated Conditions Excluding Recurrences for Children (h_cdc_t001_ex_child)
2.12	Summary of HIV Disease Progressions for Children (t_cdc_t002_child)
2.13	Summary of Last On-treatment CD4+ Cell Count Values (cell/cu mm & %) for Subjects who Prematurely Discontinue (h_cd4_disc)

Antiviral Response ICH Listings **(Note: subjects who continued after 05July2011 will be denoted with an asterisk)**

Listing	Title
7	Listing of Quantitative Plasma HIV-1 RNA Data *(h_vl_l001)*

Antiviral Response Other Listings **(Note: subjects who continued after 05July2011 will be denoted with an asterisk)**

Listing	Title
5	Listing of CD4+ Cell Count Data *(s_cd_l001)*
6	Listing of HIV Associated Conditions for Children Age <13 Years *(h_cdc_l002_child)*

Safety Tables

Table	Title
3.01	Summary of All Treatment Emergent Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (h_ae_t001_all)
3.02	Summary of All Treatment Emergent Adverse Events by System Organ Class for all study participants (h_ae_t001_all)
3.11	Summary of All Treatment Emergent Adverse Events by System Organ Class and Maximum Toxicity/Intensity for subjects who remained on treatment after 05July2011 (h_ae_t004_all)
3.12	Summary of All Treatment Emergent Adverse Events by System Organ Class and Maximum Toxicity/Intensity for all study participants (h_ae_t004_all)
3.21	Summary of All Treatment Emergent Adverse Events by System Organ Class by Age Group at Entry for subjects who remained on treatment after 05July2011 *(h_ae_t002_age)*
3.22	Summary of All Treatment Emergent Adverse Events by System Organ Class by Age Group at Entry for all study participants *(h_ae_t002_age)*
3.31	Summary of All Treatment Emergent Adverse Events by Frequency for subjects who remained on treatment after 05July2011 (h_ae_t003)
3.32	Summary of All Treatment Emergent Adverse Events by Frequency for all study participants (h_ae_t003)
3.41	Summary of Treatment Emergent Grade 2-4 Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (h_ae_t001_24)
3.42	Summary of Treatment Emergent Grade 2-4 Adverse Events by System Organ Class for all study participants (h_ae_t001_24)
3.51	Summary of Treatment Emergent Grade 2-4 Adverse Events by Frequency for subjects who remained on treatment after 05July2011 (h_ae_t003_24)
3.52	Summary of Treatment Emergent Grade 2-4 Adverse Events by Frequency for all study participants (h_ae_t003_24)
3.61	Summary of Treatment Emergent Grade 2-4 Adverse Events by System Organ Class and Age Group at Entry for subjects who remained on treatment after 05July2011 *(h_ae_t001_24_age)*
3.62	Summary of Treatment Emergent Grade 2-4 Adverse Events by System Organ Class and Age Group at Entry for all study participants *(h_ae_t001_24_age)*

3.71	Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (h_ae_t001_dr)
3.72	Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class for all study participants (h_ae_t001_dr)
3.81	Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class and Maximum Toxicity for subjects who remained on treatment after 05July2011 *(h_ae_t004_dr)*
3.82	Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class and Maximum Toxicity for all study participants *(h_ae_t004_dr)*
3.91	Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class and Age Group at Entry for subjects who remained on treatment after 05July2011 *(h_ae_t004_dr_age)*
3.92	Summary of Drug Related Treatment Emergent Adverse Events by System Organ Class and Age Group at Entry for all study participants *(h_ae_t004_dr_age)*
3.101	Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (h_ae_t001_dr_24)
3.102	Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by System Organ Class for all study participants (h_ae_t001_dr_24)
3.111	Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by Frequency for subjects who remained on treatment after 05July2011 (h_ae_t003_dr_24)
3.112	Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by Frequency for all study participants (h_ae_t003_dr_24)
3.121	Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by System Organ Class and Age Group at Entry for subjects who remained on treatment after 05July2011 *(h_ae_t001_dr_24_age)*
3.122	Summary of Drug Related Treatment Emergent Grade 2-4 Adverse Events by System Organ Class and Age Group at Entry for all study participants *(h_ae_t001_dr_24_age)*
3.131	Summary of Treatment Emergent Grade 3/4 Adverse Events by Frequency for subjects who remained on treatment after 05July2011 *(h_ae_t001_34)*
3.132	Summary of Treatment Emergent Grade 3/4 Adverse Events by Frequency for all study participants *(h_ae_t001_34)*

3.141	Summary of Treatment Emergent Serious Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 *(h_ae_t001_ser)*
3.142	Summary of Treatment Emergent Serious Adverse Events by System Organ Class for all study participants *(h_ae_t001_ser)*
3.151	Summary of Treatment Emergent Serious Adverse Events by System Organ Class and Age Group at Entry for subjects who remained on treatment after 05July2011 *(h_ae_t001_ser_age)*
3.152	Summary of Treatment Emergent Serious Adverse Events by System Organ Class and Age Group at Entry for all study participants *(h_ae_t001_ser_age)*
3.161	Summary of Drug Related Treatment Emergent Serious Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 *(h_ae_t001_dr_ser)*
3.162	Summary of Drug Related Treatment Emergent Serious Adverse Events by System Organ Class for all study participants *(h_ae_t001_dr_ser)*
3.171	Summary of Treatment Emergent Adverse Events Leading to Permanent Discontinuation of Chronic FPV for subjects who remained on treatment after 05July2011 (h_ae_t001_disc)
3.172	Summary of Treatment Emergent Adverse Events Leading to Permanent Discontinuation of Chronic FPV for all study participants (h_ae_t001_disc)
3.181	Summary of Treatment Emergent Adverse Events Leading to Withdrawal from the Study for subjects who remained on treatment after 05July2011 (h_ae_t001_wdw)
3.182	Summary of Treatment Emergent Adverse Events Leading to Withdrawal from the Study for all study participants (h_ae_t001_wdw)
3.191	Summary of All Episodes of Selected Drug Related Treatment Emergent AEs by Days to Onset, Duration, Status, Intensity and Action Taken for subjects who remained on treatment after 05July2011 (s_ae_t003)
3.192	Summary of All Episodes of Selected Drug Related Treatment Emergent AEs by Days to Onset, Duration, Status, Intensity and Action Taken for all study participants (s_ae_t003)
3.201	Summary of Treatment Emergent Rash Adverse Events by System Organ Class for subjects who remained on treatment after 05July2011 (t_ae_t002_rash)
3.202	Summary of Treatment Emergent Rash Adverse Events by System Organ Class for all study participants (t_ae_t002_rash)

3.211	Summary of Clinical Chemistry by Visit – Parameters of Special Interest by Age Group at Entry for subjects who remained on treatment after 05July2011 (h_lb_t001_chem_sp_age)
3.212	Summary of Clinical Chemistry by Visit – Parameters of Special Interest by Age Group at Entry for all study participants (h_lb_t001_chem_sp_age)
3.221	Summary of Clinical Chemistry by Visit – All Other Parameters for subjects who remained on treatment after 05July2011 (h_lb_t001_chem_oth)
3.222	Summary of Clinical Chemistry by Visit – All Other Parameters for all study participants (h_lb_t001_chem_oth)
3.231	Summary of Haematology by Visit for subjects who remained on treatment after 05July2011 (h_lb_t001_hem)
3.232	Summary of Haematology by Visit for all study participants (h_lb_t001_hem)
3.241	Summary of Clinical Chemistry Toxicities – Total for subjects who remained on treatment after 05July2011 (s_lb_t003_chem)
3.242	Summary of Clinical Chemistry Toxicities – Total for all study participants (s_lb_t003_chem)
3.251	Summary of Clinical Chemistry Toxicities – Parameters of Special Interest for subjects who remained on treatment after 05July2011 (s_lb_t003_chem_sp)
3.252	Summary of Clinical Chemistry Toxicities – Parameters of Special Interest for all study participants (s_lb_t003_chem_sp)
3.261	Summary of Clinical Chemistry Toxicities – All Other Parameters for subjects who remained on treatment after 05July2011 (s_lb_t003_chem_othf)
3.262	Summary of Clinical Chemistry Toxicities – All Other Parameters for all study participants (s_lb_t003_chem_othf)
3.271	Summary of Haematology Toxicities for subjects who remained on treatment after 05July2011 (s_lb_t003_hem)
3.272	Summary of Haematology Toxicities for all study participants (s_lb_t003_hem)
3.281	Summary of Vital Signs Data by Visit for subjects who remained on treatment after 05July2011 (h_vs_t001)
3.282	Summary of Vital Signs Data by Visit for all study participants (h_vs_t001)
3.291	Summary of Abacavir Hypersensitivity Record for subjects who remained on treatment after 05July2011 (h_abc_t001)

3.292	Summary of Abacavir Hypersensitivity Record for all study participants (h_abc_t001)
3.301	Summary of Common (≥5% Frequency) Non-Serious Treatment Emergent Adverse Events by Overall Frequency for subjects who continued treatment after 05July2011 *(h_ae_fdaaa)*
3.302	Summary of Common (≥5% Frequency) Non-Serious Treatment Emergent Adverse Events by Overall Frequency for all study participants *(h_ae_fdaaa)*
3.310	Summary of COVID-19 Assessment for Subjects with COVID-19 Adverse Events (PAN1)
3.320	Summary of COVID-19 Symptoms for Subjects with COVID-19 Adverse Events (PAN3)

Safety ICH Listings **(Note: subjects who continued after 05July2011 will be denoted with an asterisk)**

Listing	Title
8	Listing of Exposure Data *(h_ex_l001)*
9	Listing of All Adverse Events *(h_ae_l001_all)*
10	Listing of Fatal Adverse Events *(h_ae_l001_ft)*
11	Listing of Non-Fatal Serious Adverse Events *(h_ae_l001_ser)*
12	Listing of Subject Numbers for Individual Adverse Events *(h_ae_l003)*
13	Listing of Clinical Chemistry Data for Subjects with Laboratory Abnormalities *(h_lb_l001_chem_abn)*
14	Listing of Haematology Data for Subjects with Laboratory Abnormalities *(h_lb_l001_hem_abn)*

Safety Other Listings **(Note: subjects who continued after 05July2011 will be denoted with an asterisk)**

Listing	Title
7	Listing of Adverse events Leading to Permanent Discontinuation of Investigational Product *(h_ae_l001_disc)*
8	Listing of Adverse Events Leading to Withdrawal from the Study *(h_ae_l001_wdw)*
9	Listing of Adverse Events for Subjects who Experienced a Rash *(h_ae_l001_rash)*
10	Listing of Relationship of MedDRA Preferred Terms to Lower Level Terms and Adverse Event Investigator Text *(h_ae_l002)*
11	Listing of Clinical Chemistry Data *(h_lb_l001_chem)*
12	Listing of Haematology Data *(h_lb_l001_hem)*
13	Listing of Laboratory Data from Local Labs *(h_lb_l002)*
14	Listing of Vital Signs Data *(h_vs_l001)*
15	Listing of Clinical Chemistry Laboratory Data for Subjects with Laboratory Abnormalities of Potential Clinical Concern(LB5)
16	Listing of Hematology Laboratory Data for Subjects with Laboratory Abnormalities of Potential Clinical Concern(LB5)

Safety Figures

Figure	Title
3.1	Onset, Duration, Severity and Outcome of First Occurrence of AEs of Special Interest *(s_ae_f001)*
3.2	Individual patient profile plots of LFTs for Subjects who Experience a Grade 3 or 4 LFT Toxicity *(s_ae_f002)*
3.3	Individual patient profile plots of Neutrophils, Lymphocytes and White Blood Cells for Subjects who Experience a Grade 3 or 4 Neutrophil Toxicity *(s_ae_f003)*

Clinical Pharmacology Tables

Table	Title	Format /QC level
10.01	Summary of APV concentrations (mean and standard deviation, median and 95% percentile)	Table 10.1
10.02	Summary of RTV concentrations (mean and standard deviation, median and 95% percentile)	Table 10.2
10.03	Listing of Plasma APV Concentration Data (mg/mL) (by Subject and Visit)	Table 10.3
10.04	Listing of Plasma RTV Concentration Data (mg/mL) (by Subject and Visit)	Table 10.4

Viral Genotyping/Phenotyping Tables

Table	Description	Programming Note
11.01	Summary of Subject Accountability by age group: Populations *(s_vir_t001)*	
11.02	Summary of Subject Accountability Genotypic Data Available – Baseline Virology Population *(s_vir_t002_base)*	
11.03	Summary of Subject Accountability Genotypic Data Available – Virological Failure Population *(s_vir_t002_fail)*	
11.04	Summary of Subject Accountability Phenotypic Data Available – Baseline Virology Population *(s_vir_t003_base)*	
11.05	Summary of Subject Accountability Phenotypic Data Available – Virological Failure Population *(s_vir_t003_fail)*	
11.11	Summary of End of Study Record - Virological Failure Population for two groups- the confirmed virologic failure population for all subjects with confirmed virologic failures *(h_ds_t001_fail)*	
11.12	Summary of End of Study Record - Virological Failure Population for the confirmed virologic failure population after Week 48 to EoS	
11.21	Summary of Baseline Characteristics - Virological Failure Population for all subjects with Confirmed Virologic Failure *(h_dm_char_fail)*	
11.22	Summary of Baseline Characteristics - Virological Failure Population for all subjects with Confirmed Virologic Failure after Week 48 to EoS	
11.31	Summary of PR and RT Genotypic Mutations at Failure Timepoint by ART/PI Status – Virological Failure Population for the confirmed virologic failure population after Week 48 to EoS	
11.32	Summary of PR and RT Genotypic Mutations at Failure Timepoint by ART/PI Status – Virological Failure Population for all Virologic Failure(s_geno_ft_fail)	

11.41	Summary of Baseline RT and PR Mutations Associated with Each Drug Class at the virologic failure timepoint for confirmed virologic failures after Week 48 to EoS – Virological Failure Population	
11.42	Summary of Baseline RT and PR Mutations Associated with Each Drug Class at the virologic failure timepoint for all Virologic failures – Virological Failure Population *(s_geno_drg_bl_fail)*	
11.50	Summary of RT and PR Mutations by Subject and Visit – Virological Failure Population *(s_geno_subj_fail)*	*Note: Footnotes to be included * Indicates that the sample was used as part of a virological failure paired sample; # Indicates a treatment emergent mutation and ^^ after the Subject ID indicates the subject met confirmed virologic failure after Week 48 through EoS*
11.61	Summary of Treatment Emergent PR and RT Genotypic Mutations by ART/PI Status – Virological Failure Population after Week 48 to EoS	
11.62	Summary of Treatment Emergent PR and RT Genotypic Mutations by ART/PI Status – Virological Failure Population *(s_geno_te)*	
11.71	Summary of Treatment Emergent RT and PR Mutations at Failure Timepoint Associated with Each Drug Class – Virological Failure Population after Week 48 through EOS	
11.72	Summary of Treatment Emergent RT and PR Mutations at Failure Timepoint Associated with Each Drug Class – Entire Virological Failure Population *(s_geno_drg_ft)*	
11.81	Summary of Genotypic Resistance defined by IAS-USA guidelines at Baseline and Failure Timepoint by Treatment, ART/PI Status and Subject – Virological Failure Population *(s_geno_IAS pi_fail)*	Note: ^^ *after the Subject ID indicates the subject met confirmed virologic failure after Week 48 through EoS*
11.82	Summary of Genotypic Resistance defined by IAS-USA guidelines at Baseline and Failure Timepoint by Treatment, Age Group at Entry Status and Subject – Virological Failure Population *(s_geno_IAS_age_fail)*	Note: ^^ *after the Subject ID indicates the subject met confirmed virologic failure after Week 48 through EoS*

11.91	Summary of Fold Resistance by Subject and Visit - Virological Failure Population after Week 48 through EoS (s_fr_subj_fail)	Note: * indicates the sample was used as a virological failure paired sample
11.92	Summary of Fold Resistance by Subject and Visit - Entire Virological Failure Population *(s_fr_subj_fail)*	Note: * *indicates the sample was used as a virological failure paired sample*
11.101	Summary of Treatment Emergent Susceptibility at Failure Timepoint by ART/PI Status – Virological Failure Timepoint Virologic Failure Population after Week 48 through EoS	
11.102	Summary of Treatment Emergent Reduced Susceptibility at Failure Timepoint by ART/PI Status – Virological Failure Timepoint -Entire Virologic Failure Population	

Viral Genotyping/Phenotyping Listings

Listing	Title
17	Listing of Subject Accountability: Populations *(h_pn_t001_vir)*
18	Listing of Reverse Transcriptase Mutations *(h_vir_l001)*
19	Listing of Protease Mutations *(h_vir_l002)*
20	Listing of Phenotypic Data *(h_vir_l003)*
21	Summary of Phenotypic Data for On-Therapy drugs by Subject *(s_phen_drug_l001)*
22	Listing of Clade assignment *(s_clade_l001)*
23	Listing of Replicative Capacity Data *(s_rc_l001)*

16.2. Data Display Specifications

Available upon request.