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Statistical Analysis Plan

ABX464-004

A multi-centre, randomized, double-blind, placebo-controlled Phase IIa trial to compare the safety of ABX464 given at a fixed dose to placebo in fully controlled HIV infected patients treated with boosted protease inhibitor treatment (darunavir/ritonavir or darunavir/cobicistat)

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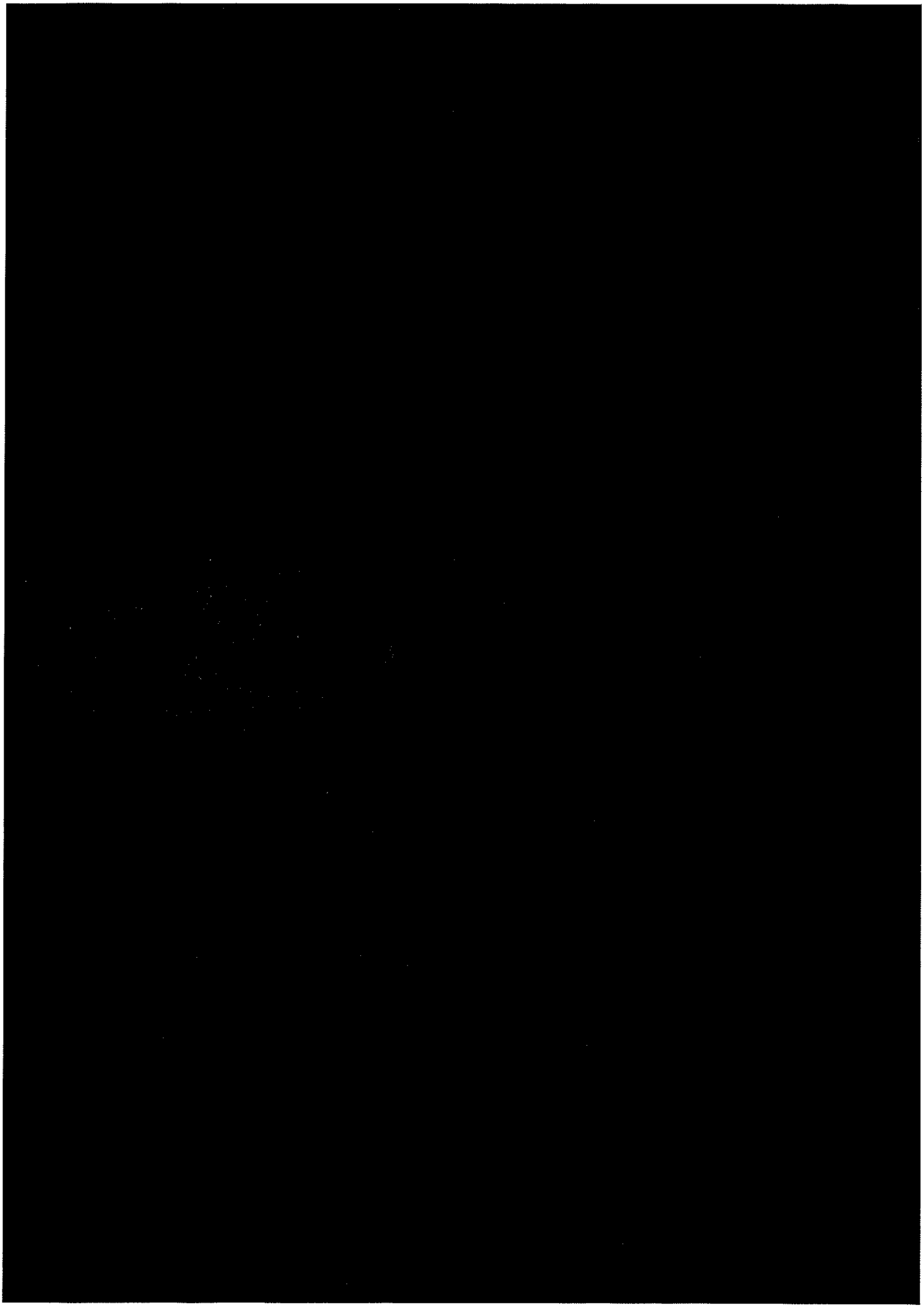

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GLOSSARY OF ABBREVIATIONS

%CV	Coefficient of Variation
AE	Adverse Event
ALT	Alanine Transaminase (also SGPT)
AM	Arithmetic Mean
ANOVA	Analysis of Variance
ART	Anti-Retroviral Therapies
AST	Aspartate Transaminase (also SGOT)
ATC	Anatomical Therapeutic Chemical
AUC	Area Under the Plasma Concentration Curve
AUC τ	Area Under the Plasma Concentration-time Curve calculated over one dosing interval at steady state
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
Cmax	Maximum observed plasma concentration
COBI	Cobicistat
CR	Complete Response
CRF	Case Report Form
CRO	Clinical Research Organisation
CS	Clinically Significant
CSR	Clinical Study Report
CTCAE	Common Toxicity Criteria Adverse Event
CV	Coefficient of Variation
DBL	Database Lock
DLT	Dose Limiting Toxicity
DMP	Data Management Plan
DOB	Date of Birth
DRM	Data Review Meeting
DRV	Darunavir

DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
FAS	Full Analysis Set
gGT	Gamma-Glutamyl-Transferase
GM	Geometric Mean
ICH	International Conference on Harmonisation
IMP	Investigational Medicinal Product
LDH	Lactate Dehydrogenase
LLQ	Lower Limit of Quantification
LS Mean	Least Squares Mean
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
ml	Millilitre
N	Number of Patients
n	Number of Events
NCS	Not clinically significant
od	Once daily
PBMC	Peripheral Blood Mononucleated Cells
PD	Pharmacodynamics
PK	Pharmacokinetics
PP	Per Protocol
PR	Partial Response
PT	Preferred Term
QC	Quality Control
RBC	Red Blood Cell
RTV	Ritonavir
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SE	Standard Error
SOC	System Organ Class

TEAE	Treatment Emergent Adverse Event
tmax	Time from dosing to the maximum observed plasma concentration
VR	Viral Rebound
WBC	White Blood Cell
WHO	World Health Organisation
WHODD	World Health Organisation Drug Dictionary
µg	Microgram

1 INTRODUCTION

1.1 GENERAL

This statistical analysis plan (SAP) describes the statistical methods to be used during the reporting and analyses of data collected under Abivax Protocol ABX464-004 and should be read in conjunction with the study protocol and electronic case report form (eCRF).

This version of the plan has been developed using the protocol Version 4.0 dated 7NOV2016 and annotated CRF Version 4.0 dated 21DEC2016. Any further changes to the protocol or CRF will be reviewed for potential impact on the SAP which will be amended if it is deemed necessary.

1.2 CHANGES FROM THE PREVIOUS SAP

The dose escalation from 50mg o.d. to 150mg o.d. has been recommended by the DSMB.

2 STUDY OBJECTIVES

2.1 PRIMARY OBJECTIVE

To evaluate the safety of ABX464 versus placebo when administered on top of darunavir/ritonavir or darunavir/cobicistat monotherapy.

2.2 SECONDARY OBJECTIVES

- To evaluate the long-lasting effect of ABX464 on the viral load after treatment stop (Day 29) using the time to Viral Rebound (VR) versus placebo;
- To compare the effect of ABX464 on viral load (HIV RNA) versus placebo from Day 0 to VR;
- To compare the effect of ABX464 on the CD4+ T cell counts versus placebo from Day 0 to VR;
- To compare the effect of ABX464 on the CD4+/CD8+ T cells ratio versus placebo from Day 0 to VR;
- To evaluate the effect of ABX464 on HIV reservoir (pro-viral DNA in peripheral blood mononucleated cells [PBMC]) versus placebo from Day 0 to VR;

The following secondary efficacy variables are mentioned in the protocol but will not be part of the clinical database, and so will not be analysed as part of this SAP.

- To assess the Pharmacokinetics (PK) parameters of ABX464 given on top of darunavir/ritonavir/cobicistat;

- To compare the effect of ABX464 on miRNA modulations and tropism of HIV versus placebo from Day 0 to VR.

3 STUDY DESIGN

3.1 OVERVIEW

This study is a placebo-controlled study aimed at assessing the safety of ABX464 administered at 50 mg o.d. (or potentially at 150 mg o.d.) versus placebo in HIV infected patients who are treated with darunavir (DRV) and ritonavir (RTV) or DRV and cobicistat (COBI).

Patients will be recruited to 8 sites in France, Spain and Belgium from Q1 2016 – Q2 2016 during the overall study period of Q4 2015 – Q3 2016. Patients will be randomised using a 3:1 ratio, where per treatment block, 3 patients will be randomised to receive ABX464 and 1 patient will be randomised to receive placebo. A total of 28 evaluable patients are required at a dose level: 21 patients in the ABX464 at 50mg/150mg group and 7 patients in the placebo group.

In November 2015, the original fixed dose of 50mg o.d. was selected based on safety data accumulated on the 50mg o.d. regimen and the concentrations in ABX464-N-glucuronide (NGlcABX464), the active metabolite of ABX464. However, in January 2016, the results of a first phase IIa study conducted in treatment-naïve HIV infected patients with high viral load at enrolment (5,000 - 500,000 copies/mL) confirmed the antiviral activity of ABX464 at higher doses. A reduction of viral load >0.5 log was observed in 3/12 patients in the 75mg and 100mg cohorts and 4/6 patients in the 150mg cohort, demonstrating a dose relationship effect of ABX464.

In this study, if the first 8 patients treated at 50mg o.d. for 28 days (first 2 randomisation blocks) do not show a dose limiting toxicity (DLT), the study protocol plans to study the 150mg dose. DLT is defined as a grade 3 or higher adverse event, as defined by the "Division of AIDS table for grading the severity of adult and paediatric adverse events" (including signs/symptoms, lab toxicities and/or clinical events), considered by the Data Safety Monitoring Board (DSMB) as probably or definitely related to study treatment. The DSMB will meet once the first 8 patients have been treated for 28 days in order to recommend a dose increase to 150mg o.d., if appropriate.

If the dose escalation to 150mg o.d. is recommended, the sample size at dose level will not be changed and a total of 28 patients will need to be randomised to the new dose. Therefore, the overall sample size can vary from 28 patients if the dose escalation is not recommended (28 patients taking 50mg o.d.) to 36 patients if the dose escalation is recommended (8 patients taking 50mg o.d. and 28 patients taking 150mg o.d.).

3.2 INCLUSION AND EXCLUSION CRITERIA

To be eligible for inclusion into this study, each patient must fulfil all inclusion criteria and not violate any exclusion criteria (for the protocol under which they are entered) during screening prior to randomisation. Details of the inclusion and exclusion criteria are presented in the protocol.

3.3 Study Treatment

All patients must be treated with DRV and one of either RTV or COBI for at least 8 weeks prior to baseline and during the course of the study until Day 28 at following doses:

- 800mg of DRV and 100mg of RTV once a day with food or;
- 800mg of DRV and 150mg of COBI once a day with food.

ABX464 or matching placebo should be administered once daily at a fixed dose of 50 mg (or 150 mg o.d. if the dose escalation is recommended) from Day 1 to Day 28.

At Day 29, all treatments of DRV and RTV/COBI and ABX464 or its matching placebo will be stopped. The viral load will be monitored and when VR is reached, defined as HIV viral load > 1,000 copies mL-1, the anti-retroviral therapies (ART) will be resumed.

3.4 Study Timepoints

There is a 2 to 4 week screening period followed by a 4 week treatment period that consists of 5 visits.

All treatments will be stopped at Day 29 and the viral load will be monitored twice a week during the first three weeks and weekly during the next weeks. The treatment interruption period will last until the viral load rebounds (VR) at which point ART use will resume and the patient will be withdrawn from the study. After ARTs are re-introduced, a follow up visit is required every 14 days until the viral load has returned to undetectable levels.

Overall, the minimal study duration for any patient will be 49 days.

In case of no VR then the end of study will be 3 months after treatment interruption with the possibility for the patient to be enrolled in long term-observational follow-up study.

Visits and visit windows will be as follows:

Visit	Study Day	Window
Screening	-21	± 7 days
Randomisation	0	± 2 days
Treatment period	7	± 2 days
	14	± 2 days
	21	± 2 days
	25	± 4 days
	28	± 2 days
Treatment interruption		
Viral load monitoring twice a week for 3 weeks		± 2 days
Viral load monitoring every week until VR		± 2 days

ART reintroduction visit	± 2 days
Follow up visits	
Follow up visit every 14 days till undetectable viral load	± 2 days

If more than one visit occurs within a window, the nearest to the scheduled time will be presented within the summaries.

See Section 16.1 for the Study Flow Chart.

3.5 Sample Size Considerations

The endpoint considered for the sample size calculation is the time to VR defined as the time between treatment stop (Day 29) and VR detection, measured in days.

According to published studies, the expected median time to VR (calculated from treatment stop) is expected to be 7 days in the DRV and RTV/COBI and placebo group while it should be at least 28 days in the DRV and RTV/COBI and ABX464 group in order to continue the clinical development of this new drug.

According to these hypotheses, the corresponding power was calculated using the PROC POWER of the SAS software (version 9.4). Thus, the enrolment of 28 evaluable patients at a dose level (21 in the ABX464 group at 50 mg or 150 mg and 7 in the placebo group) will permit to have 80% power to detect a significant difference, at 0.05 level, between groups using the time to VR as end point.

Thus, the overall sample size can vary from 28 patients (in case the dose escalation procedure is not recommended) to 36 patients in case the dose escalation to 150 mg o.d. is recommended.

3.6 Randomisation

Patients will be randomised using a 3:1 ratio, where for each block of 4 patients, 3 patients will be randomised to receive ABX464 and 1 patient will be randomised to receive placebo. A total of 28 evaluable patients are required at a dose level: 21 patients in the ABX464 at 50mg/150mg group and 7 patients in the placebo group.

Randomisation will be performed via the eCRF and will allocate treatment number assignment. The treatment bottle numbers to be used for a specific patient will be assigned according to a pre-defined randomisation list by SODIA. This information will be provided to sites by e-mail or fax.

4 STUDY VARIABLES

4.1 Primary Variable

The primary variable for statistical comparison between treatment groups will be time to VR (days), defined as the time between end of treatment (Day 29) and VR detection.

4.2 Secondary Efficacy Variables

The following secondary efficacy variables will be analysed between treatment groups:

- Viral load (HIV RNA) from Day 0 to VR (on both the linear and log_{10} scale);
- CD4+ T cell counts from Day 0 to VR;
- CD4+/CD8+ T cells ration from Day 0 to VR;
- HIV reservoir (pro-viral DNA in PBMC) from Day 0 to VR;

The following secondary efficacy variables are mentioned in the protocol but will not be part of the clinical database, and so will not be analysed as part of this SAP.

- miRNA modulations and HIV tropism from Day 0 to VR.

4.3 Pharmacokinetic Variables

Pharmacokinetic data will not be part of the clinical database, and so will not be analysed as part of this SAP.

4.4 Safety Variables

The safety of ABX464 versus placebo when administered on top of DRV and RTV/COBI monotherapy will be evaluated by the following:

- Adverse events
- Laboratory parameters
- Vital signs (weight, body temperature, systolic and diastolic blood pressure, heart rate)
- ECG (normal, abnormal NCS or abnormal CS)

5 DEFINITIONS

Study Drug. Study drug is taken to mean either ABX464 or placebo.

Baseline. Baseline is defined by patient and by variable as the last non-missing value before the first dose of study drug.

Study Day. Study day is the number of days since start of treatment where the date of first dose is counted as Day 1.

Evaluable. Evaluable is defined in the protocol and is a guide to the need for continued recruitment. The term is not used in the statistical context, but is approximately equivalent to the set of patients with a result for the primary efficacy endpoint.

Protocol Deviation: a deviation related to study inclusion or exclusion criteria, conduct of the trial, patient management or patient assessment. This refers to any change, divergence, or departure from the study design or procedures defined in the protocol. Deviations recorded by the Project Manager

or CRA, or detected by data management or by statistical programming checks will be identified and discussed at the Data Review Meeting (DRM) before database lock (DBL) to agree which should be included in Listing 16.2.2.

Major Protocol Deviation: These are defined as protocol deviations that are liable to bias the evaluation of the main efficacy endpoint. The following deviations will be considered as major (non-exhaustive list):

- Non-compliance with the inclusion or exclusion criteria;
- Non-compliance with the study treatment;
- Intake of prohibited medication;
- Non-compliance with time window.

6 ANALYSIS SETS

Membership of the analysis sets will be reviewed and agreed at a DRM before database lock.

6.1 FULL ANALYSIS SET

The Full Analysis Set (FAS) is defined as those patients who have received at least one dose of the study drug, and who have at least one baseline value.

The FAS will be used for all efficacy analyses. Patients who receive the wrong treatment in error will be analysed as randomised for efficacy analyses.

6.2 SAFETY SET

The safety set is defined as all randomised patients who have received at least one dose of study drug.

The safety set will be used for all safety analyses. Patients who receive the wrong treatment in error will be analysed as treated for safety analyses.

6.3 PER PROTOCOL SET

The Per Protocol (PP) set (except for the analysis of HIV reservoirs), is defined as those patients of the FAS population without any major protocol deviation.

The PP set for analysis of HIV reservoirs is defined as patients with a total HIV DNA $\geq$ 50 copies at any time point and without any major protocol deviation.

All primary efficacy analysis will be repeated using the PP set. If there are less than 3 exclusions in the ABX464 group and less than 1 exclusion in the placebo group from the FAS, the tables using the PP set will not be produced.

7 SAFETY MONITORING

No safety monitoring reports are planned.

An independent DSMB will review the data in a blinded fashion during the study and can make recommendations to the sponsor.

8 INTERIM ANALYSES

No interim analysis is planned.

9 DATA

9.1 eCRF DATA

CRF data will be provided by Orion data management to the statistics department as SAS data sets in Orion standard format which will be used for programming the outputs to be included in the CSR. Populated data sets will be available when programming starts. These may contain dummy data if real data is not yet available.

9.2 EXTERNAL DATA

HIV reservoir data will be analysed centrally by University Hospital Ghent, Belgium and sent to Orion in the form of SAS datasets.

No other external data will be received by Orion. In particular, no miRNA modulations, HIV tropism or PK data will be received or analysed by Orion.

9.3 RANDOMISATION LIST

The randomisation list will be uploaded to a SAS dataset following database lock.

9.4 PROGRAMMING AND DATA REVIEW

Programming of analysis datasets, tables, figures and listings will be ongoing during the data management of the study. Outputs for the DSMB will be reviewed, but no formal quality control (QC) will take place. Blind outputs may be reviewed by Abivax before DBL.

When the final data is considered clean, key listings (to be agreed) will be run and distributed to the study team for review. A blind DRM will be held to discuss the outcome of this review, the imputations for the primary endpoint and the protocol deviations. Once all data issues have been resolved and the analysis populations approved, the database will be locked. The final run of outputs and QC will then take place.

10 STATISTICAL METHODS

10.1 GENERAL PRINCIPLES

All statistical methods will be based on the International Conference on Harmonisation (ICH) E9 document "Statistical Principles for Clinical Trials".

Data will be summarised by treatment group. A total column showing all patients will be included for baseline and safety summaries. Where appropriate, data will also be summarised by visit with summaries for each visit attended as scheduled and an additional summary for final (last scheduled visit or early withdrawal). The format of the summaries is defined in the shells at the end of this document.

All summary tables will be made up of the following three columns:

- Patients receiving the 50mg dose of ABX464;
- Patients receiving the 150mg dose;
- Patients receiving placebo.

In addition, summary tables for total DNA will be made up with an additional column of the two active dose regimens pooled.

All treatment comparisons in efficacy will be conducted between 150mg dose and placebo only, where placebo includes all patients randomised to placebo regardless of the dose they were enrolled to.

In summary and analysis tables of continuous variables, standard descriptive statistics (N, mean, standard error [SE], standard deviation [SD], median, quartiles, minimum, maximum and N missing) will be presented when relevant. Least Squares mean (LS mean), SE and 95% confidence Interval (CI) will be presented in the statistical analysis outputs as appropriate. For PK summaries, arithmetic mean (AM), geometric mean (GM) and coefficient of variation (%CV) will be used to summarise the data. The minimum and maximum statistics will be presented in summary tables to the same number of significant figures as the original data. The mean/AM, median, LS mean, GM, CI, SD and SE will be presented to one more significant than the original data.

For numeric data which includes non-numeric values (e.g. PK data reported as BLQ or lab results reported as < 10 or >100) the following principles will be applied when summarising the data:

- BLQ will be replaced with a value that is ½ of the lower limit of quantification (LLQ)
- Results reported as < x will be treated in the same way as BLQ with LLQ=x
- Otherwise AM, GM, SD, CI and %CV will not be calculated
- Whenever meaningful, minimum, median and maximum will be presented based on the reported data (e.g. minimum = <10, median = 20, maximum = >100)

In summary tables of categorical variables, the number of non-missing observations by category will be presented with percentages. The number of missing observations will also be presented when non-zero. Unless otherwise specified, the denominator for each percentage will be the number of non-missing observations within the column. All percentages will be presented to one decimal place.

If changes in severity for the same TEAE have been reported separately but with the same AE number, they will be collapsed to a single AE with maximum severity for the summary tables, but listed as reported.

Classifications of medical history, concomitant medication and adverse events will be sorted alphabetically within the summary tables.

If any laboratory assessments are repeated at the same visit, the result from the repeat assessment will be used in summaries. Both values will be listed.

Data collected on the eCRF will be presented within data listings. The data listings will be sorted by treatment group, country, centre number, patient number and visit/week/day. Treatment group will be as allocated (randomised). If any patients receive the wrong treatment this will be flagged in all listings. Visits outside the visit windows will be identified within the listings.

The date format for all output presentations will be 'ddMMMyyyy'.

All statistical analysis will be performed using SAS 9.3 or higher.

All hypothesis testing will be carried out at the 5% (2-sided) significance level unless stated otherwise.

P-values will be rounded to four decimal places. P-values less than 0.0001 will be reported as <0.0001 in tables.

If any of the assumptions underlying the formal statistical methods proposed are violated during the analysis of the final data, alternative statistical methods will be used and any changes documented in the statistical methods section of the clinical study report (CSR), including the rationale for use.

10.2 Missing Data

There will be no imputation of missing data in this study.

10.3 Pooling of Sites

Sites will be pooled for all analyses. There will be no adjustment for centre effect or treatment by centre interaction.

10.4 Statistical Issues

Since the dose escalation to 150mg o.d. has been recommended, all patients receiving placebo, regardless of which dose they were enrolled to, will be gathered in a placebo group accounting for a theoretical total of a minimum of 7 patients. However, only patients receiving the 150mg dose will be compared to placebo and included in the efficacy analysis.

11 STATISTICAL OUTPUT

General principles for layout of the statistical output are described in Section 10.1, including specification of the table columns, and these are illustrated for each unique table in the table shells in

Section 15. For clarity and brevity in this document the phrase "by treatment group" is understood for all summaries and is not included within the text of this section.

The study analysis will be performed following database lock upon the completion of the last patient or upon its early discontinuation whichever occurs first.

11.1 PATIENT DISPOSITION

A patient is considered to be a baseline failure if the patient signs the informed consent but withdraws before the screening visit. Reasons for exclusion will be recorded for patients who do not enter the study and presented in a data listing.

A patient who does not fulfil the randomisation criteria at Day 0 will be considered as a screen failure.

A summary of the number of screened patients, baseline failures, screening failures and reasons for screening failure will be produced for all enrolled patients *(Table 14.1.1)*.

The number (%) of patients who complete or withdraw from the study and the main reason for withdrawal will be summarised for all randomised patients *(Table 14.1.2)*.

The patient disposition table *(Table 14.1.3)* will summarise the following data for all randomised patients:

- The number (%) of patients in the FAS
- The number (%) of patients in the safety set
- The number (%) of patients in the PP set

A data listing presenting the eligibility for the analysis sets for each patient will also be presented.

Protocol deviations will be reviewed and classed as major or minor during the blind DRM. A listing of all patients with protocol deviations will be presented.

11.2 PATIENT CHARACTERISTICS AT BASELINE

11.2.1 Demographic and Baseline Characteristics

Age will be calculated using Date of Birth (DOB) and date of informed consent and presented as age at last birthday as an integer.

BMI is the patient's body weight in kilograms divided by the square of the patient's height in metres.

Age, gender, race, height, weight and BMI will be summarised using the FAS *(Table 14.1.4)*.

11.2.2 Medical History and Current Medical Conditions

All conditions will be coded using the version of the Medical Dictionary for regulatory Activities (MedDRA) defined in the Data Management Plan (DMP). Past medical/surgical history (conditions that stopped prior to or at the screening visit) and current medical conditions (classified as 'ongoing') will be summarised by system organ class (SOC) and preferred term (PT). The number (%) of patients reporting each condition will be presented using the FAS *(Table 14.1.5.1 and 14.1.5.2)*.

11.2.3 Procedures/Non-Drug Therapies

All procedures/non-drug therapies recorded on the CRF will be listed only.

11.3 EFFICACY ANALYSES

Treatment comparisons will be ABX464 vs placebo. The main analysis set for the efficacy analyses will be the FAS, and the primary analysis will be repeated for the PP Set.

11.3.1 Primary Efficacy Analysis

The primary endpoint, time to VR (days), defined as the time between end of treatment (date of last dose) and VR detection will be descriptively summarised on the FAS set *(Table 14.2.1.1.1)* and displayed graphically using the Kaplan-Meier method *(Figure 1)*.

The median time to VR (days) for each treatment and the corresponding 2-sided 95% confidence interval (CI) will be presented along with a 2-sided log-rank test to compare time to VR between the two treatments *(Table 14.2.1.1.1)*.

The primary endpoint analysis will be repeated for the PP set *(Table 14.2.1.1.2)*.

The time to virological failure (days), defined as the time from end of treatment (date of last dose) to when HIV viral load ≥ 500 copies mL-1, will be descriptively summarised on the FAS set *(Table 14.2.1.2.1)* and displayed graphically using the Kaplan-Meier method *(Figure 2)*.

The median time to virological failure (days) will be analysed in the same way as the primary endpoint and repeated for the PP set *(Table 14.2.1.2.1 and 14.2.1.2.2)*.

11.3.2 Secondary Efficacy Analysis

11.3.2.1 Viral Load

Viral load is assessed at all visits during the treatment period (Day 0, 7, 14, 21, 25, 28), twice a week during the first three weeks after treatment interruption, and then once a week until VR detection.

Viral load will be descriptively summarised and analysed using an analysis of variance (ANOVA) model with treatment as a fixed effect, for all visits from Day 0 (baseline) to VR on the FAS set *(Table 14.2.2.1.1)*. This table will be repeated for viral load values transformed to the logarithmic scale (*Table 14.2.2.1.2*).

The time to viral load control, defined as the time from ART reintroduction to when the viral load < 50 copies mL-1, will be descriptively summarised on the FAS set (*Table 14.2.2.1.3*),

11.3.2.2 CD4+ T Cell Counts

CD4+ T cell counts are assessed at all visits during the treatment period (Day 0, 7, 14, 21, 25, 28), twice a week during the first three weeks after treatment interruption, and then once a week until VR detection.

CD4+ T cell counts will be descriptively summarised and analysed using the method outlined for viral load analysis in section 11.3.2.1 *(Table 14.2.2.2)*.

11.3.2.3 CD4+/CD8+ T Cell Count Ratio

CD4+/CD8+ T cell count ratio is derived on the eCRF at all visits during the treatment period (Day 0, 7, 14, 21, 25, 28), twice a week during the first three weeks after treatment interruption, and then once a week until VR detection.

CD4+/CD8+ T cell count ratios will be descriptively summarised and analysed using the method outlined for viral load analysis in section 11.3.2.1 *(Table 14.2.2.3)*.

11.3.2.4 HIV reservoirs

Total HIV DNA (copies/million PBMC) is assessed at Day 0, 28 and the ART reintroduction visit and will be descriptively summarised at all visits, by dose and by pooled dose *(Table 14.2.2.4.1)*.

The mean change in absolute value from Day 0 to Day 28 and the percentage change will be descriptively summarised, by dose and by pooled dose *(Table 14.2.2.4.2)*. The total HIV DNA values at Day 0 and Day 28 will be transformed to the logarithmic scale and changes calculated on this scale. Percentage change on this scale will be summarised in the same table. This table will be repeated for mean change from Day 28 to ART reintroduction visit (*Table 14.2.2.4.3*).

Patients who achieve a decrease in total DNA of ≥ 25% and a decrease to ≤ 50 copies/million PBMC from Day 0 to Day 28 are defined as responders and the number (%) of responders will be summarised. Non-responders are defined as patients without a decrease in total DNA of ≥ 25% and total DNA > 50 copies/million PBMC at Day 28, or those with missing total DNA values at Day 28.

An analysis of responders will be conducted using a binomial confidence interval for the difference in response rates on the full analysis set and repeated on the PP set for HIV reservoir data (*Tables 14.2.2.4.4 and 14.2.2.4.5*).

11.4 SAFETY ANALYSES

11.4.1 Adverse Events

All adverse events (AE) will be classified using the version of the MedDRA coding dictionary specified in the DMP.

Events will be classified as treatment-emergent if they started or increased in severity on or after the first date and time of medication dosing at Day 1 and up to Day 28, or withdrawal date if the patient discontinues before Day 28. If an event start date is partial, then the start day, month, year or stop date will be used to determine if the event is treatment-emergent. If the classification of the AE cannot be determined from the data available, then the event will be considered treatment-emergent.

Any adverse event which occurs after Day 28 will be classified as post-treatment-emergent.

An overall summary table will be presented using the safety set for adverse events occurring from baseline to the end of the study in the following categories *(Table 14.3.1)*:

- Any adverse event;
- Any treatment-emergent adverse event (TEAE);
- Any post-treatment-emergent adverse event;
- Any serious adverse event;
- Any severe adverse event (Common Toxicity Criteria [CTC] grade 3 or 4);
- Death

TEAEs will be further classified and summarised as follows *(Table 14.3.2)*:

Severe TEAEs: Severity classified as 'Grade 3', 'Grade 4' or missing.

Serious TEAEs: Serious classified as 'yes' or missing.

Drug-related TEAEs: Relationship to study drug classified as 'yes' or missing.

Serious drug-related TEAEs: Both serious and drug-related, as specified above.

TEAEs leading to study drug discontinuation: Action taken classified as 'permanent discontinuation'.

Summaries by system organ class (SOC) and preferred term (PT) will also be presented for treatment-emergent events *(Table 14.3.3.1)*. Similar tables will be presented for each of the classifications of treatment-emergent events above *(Table 14.3.3.2 to 14.3.3.6)*.

A summary of the mean duration (days) of treatment-emergent events will also be presented by SOC and PT, along with the number of events (*Table 14.3.3.7*). Duration of an event is calculated as (stop date of event - start date of event) + 1. If an AE is ongoing then use the end of study date (or last known visit date for early termination) as the stop date.

All AE summary tables, unless otherwise specified, will show the number (%) of patients having at least one event and the number of events in each treatment group and overall. Note: If a patient has multiple AEs with the same preferred term, these will be summarised once within the count for N (%) of patients, but each event will be counted within the number of reports E of each AE. Changes in severity of the same AE (if collected) will be counted only once within the number of reports E of each AE.

All adverse events recorded on the CRF will be listed by SOC and PT within the data listings.

11.4.2 Laboratory Data

Routine clinical laboratory results will be carried out at screening, all visits during the treatment period (Day 0, 7, 14, 21, 25, 28), and then once a week until VR detection and ARTs are reintroduced. The laboratory parameters include:

- Haematology: haematocrit, haemoglobin, white blood cell (WBC) count, neutrophils, lymphocytes, monocytes, eosinophils, basophils and platelet count
- Biochemistry: sodium, potassium, chloride, calcium, phosphate, glucose, blood urea nitrogen (BUN), creatinine, AST, GLDH, ALT, alkaline phosphatase, total bilirubin, total protein, albumin, lactate dehydrogenase (LDH), gamma-glutamyl-transferase (gGT) and CRP
- Urinalysis

Laboratory parameters will be summarised at each visit using descriptive statistics on the safety set *(Tables 14.3.4.1 to 14.3.4.3)*. Laboratory parameters classified as normal/ abnormal non clinically significant (NCS)/ abnormal clinically significant (CS) will be presented in a shift table showing changes from baseline to each visit for patients with at least one abnormal CS value *(Tables 14.3.5.1 to 14.3.5.3)*. Baseline is defined as the last non-missing value before the first dose of study drug, which is Day 0.

Note that urinalysis parameters collected as normal/ abnormal NCS/ abnormal CS only will be summarised in the shift tables and not as part of the summary of urinalysis parameters in Table 14.3.5.3 which will only include the parameters recorded as numeric values.

If laboratory results are repeated at the same visit, the repeated result will be used in summaries (instead of the original one) provided the sample was taken within the visit window, otherwise the original result will be used. All results will be listed.

Laboratory results at unscheduled visits will be included in the listings but will not be summarised.

For all female patients of childbearing potential, a blood pregnancy test (β-HCG) will be performed at Day 0 and then a urine pregnancy test will be performed at each visit until VR. Results of all pregnancy testing will be listed only.

11.4.3 Vital Signs

Body temperature, blood pressure, heart rate and weight are collected at all visits.

Vital signs, including body mass index (BMI), will be summarised for each visit using descriptive statistics on the safety set *(Table 14.3.6)*. Height is collected at screening and will be summarised within the demography data only.

11.4.4 Physical Examination

A physical examination will be conducted at all visits.

Physical examination data will be listed only.

11.4.5 Electrocardiogram

A 12-lead ECG will be completed at Day 0, Day 7, Day 28 and ART reintroduction visit and, if clinically indicated, at follow-up.

The number and percentage of the patients with Normal / Abnormal NCS / Abnormal CS ECG results will be summarised at each visit *(Table 14.3.7.1)*.

A shift table will be presented, for patients with at least one Abnormal CS value, showing changes from baseline to each visit *(Table 14.3.7.2)*. Baseline is defined as the last non-missing value before the first dose of study drug, which is Day 0.

11.5 Study Drug Exposure and Compliance

Study drug exposure: Exposure is the number of days during the treatment period that the patient was exposed to the study treatment and is calculated as:

- (Date of last dose) – (Date of first dose) + 1

Compliance. Compliance is derived for each patient from their date of first dose to last dose as:

- Compliance (%) = (number of administered doses / scheduled number of doses) x 100%

Number of administered doses, study drug exposure and compliance (%) will be summarised using descriptive statistics for the FAS *(Table 14.3.8)*.

11.6 Prior and Concomitant Medication

All medications taken by patients on entry to the study or during the study will be recorded in the CRF. Medications will be classified using the version of the World Health Organisation Drug Dictionary (WHODD) coding dictionary defined in the DMP. The Anatomical Therapeutic Chemical (ATC) Classification and WHO-DRUG PT will be used to list and summarise the data.

Prior medications are defined as all medications that started and stopped before date of first dose. Only medications where the stop date is prior to date of first dose will be considered prior. If the stop

date is unknown or incomplete and the medications cannot definitely be considered as stopped prior to date of first dose then the medications will be considered as maintained medications.

Maintained medications are defined as all medications that started before date of first dose and their stop date is either ongoing at the end of the study or the stop date is on or after date of first dose. Partial start dates where the medication cannot definitely be considered as starting prior to date of first dose will lead to a categorisation of the medications as concomitant medications.

Concomitant medications are defined as all medications that started on or after date of first dose.

The number (%) of patients reporting the use of any prior medications and the number (%) of patients taking each drug by ATC classification (1st, 2nd and 4th levels) and PT will be summarised using the safety set *(Table 14.3.9.1)*.

This table will be repeated for maintained and concomitant medications *(Table 14.3.9.2 and 14.3.9.3)*.

12 VALIDATION

All tables, figures and listings will be subject to independent quality control and visual review. Unique tables will be independently programmed. Findings will be documented in a quality control form and actions taken will also be documented.

The completed form will be reviewed and signed by both programmers and by the Head of Statistics.

13 LITERATURE CITATIONS/REFERENCES

None

14 LIST OF TABLES, FIGURES AND LISTINGS

14.1 LIST OF TABLES

Demographic Data

Table 14.1.1	Screening Failures	All Enrolled Patients
Table 14.1.2	Study Termination and Primary Reason for Withdrawal	All Randomised Patients
Table 14.1.3	Patient Disposition	All Randomised Patients
Table 14.1.4	Demographic and Baseline Characteristics	Full Analysis Set

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Efficacy Data

Table 14.2.1.1.1	Time to Viral Rebound Analysis	Full Analysis Set
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Table 14.2.2.4.2	Mean Change in Total HIV DNA: Day 0 vs Day 28	Full Analysis Set
Table 14.2.2.4.3	Mean Change in Total HIV DNA: Day 28 vs ART reintroduction	Full Analysis Set
Table 14.2.2.4.4	Total HIV DNA Analysis	Full Analysis Set
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Safety Data

Table 14.3.1	Summary of Adverse Events	Safety Set
Table 14.3.2	Summary of Treatment-Emergent Adverse Events	Safety Set
Table 14.3.3.1	Treatment-Emergent Adverse Events, by SOC and PT	Safety Set
Table 14.3.3.2	Severe Treatment-Emergent Adverse Events, by SOC and PT	Safety Set
Table 14.3.3.3	Serious Treatment-Emergent Adverse Events, by SOC and PT	Safety Set
Table 14.3.3.4	Drug-Related Treatment-Emergent Adverse Events, by SOC and PT	Safety Set
Table 14.3.3.5	Serious Drug-Related Treatment-Emergent Adverse Events, by SOC and PT	Safety Set
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Table 14.3.3.7	Mean Duration of Treatment-Emergent Adverse Events, by SOC and PT	Safety Set
Table 14.2.4.1	Summary of Haematology Parameters	Safety Set
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Table 14.2.5.1	Shift Table of Haematology Parameters	Safety Set
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Table 14.3.6	Vital Signs, including Weight and BMI	Safety Set
Table 14.3.7.1	12-Lead Electrocardiogram	Safety Set
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Table 14.3.9.3	Concomitant Medications	Full Analysis Set

14.2 List of Figures

Figure 1	Kaplan-Meier Plot of Time to Viral Rebound	Full Analysis Set
Figure 2	Kaplan-Meier Plot of Time to Virological Failure	Full Analysis Set

14.3 List of Listings

Patient Data Listings

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Listing 16.2.2	Protocol Deviations
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Listing 16.2.4	Demographic Data
Listing 16.2.5	Study Drug Exposure and Compliance
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Listing 16.2.8.1	Laboratory Measurements: Haematology
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15 SHELLS FOR TABLES, FIGURES AND LISTINGS

The intended layouts for tables, figures and listings are presented. However, it may be appropriate for the Orion programmer to change the layouts, upon review of the data available, for completeness and clarity.

QCd output will be produced as Rich Text Format (.rtf) files for convenient inclusion in the CSR.

Subject to this, the following will apply:

- Layout will be landscape, fixed width, font size 8.
- Each output will have the heading:

  <Client Protocol Number> (left); date ddMMMyyyy (right)
- Table headings will define the analysis set used for the summary/analysis.
- All outputs will have a footer specifying the SAS program path and filename (left); page x/y (right)
- Tables will have a footer specifying the source listing

- Figures will have a footer specifying the source table or listing
- Additional footnotes will be included where appropriate for clarification.
- Treatment group and patient number and will be included in all listings.

ABX464-004

ddMMMyyyy

Table 14.1.1 Screening Failures (All Enrolled Patients)

	Total Enrolled (N=xx)
Total number of Enrolled	xx
Randomised	xx (xx.x%)
Screening failure	xx (xx.x%)
Baseline failure	xx (xx.x%)
Primary Reason for screening failure	
Inclusion criterion not met	xx (xx.x%)
Exclusion criterion	xx (xx.x%)
Withdrawal by patient	xx (xx.x%)
Other	xx (xx.x%)

The denominator for each percentage is the number of enrolled patients

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ABX464-004 ddMMMyyyy

Table 14.1.2 Study Termination and Primary Reason for Withdrawal (All Randomised Patients)

	50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Total (N=xx)
Randomised	xx	xx	xx	xx
Completed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Early withdrawal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Main reason for early withdrawal				
Investigator's decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Adverse event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Major protocol violation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patient's decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawal of consent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to follow-up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The denominator for each percentage is the number of randomised patients in the column

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ABX464-004 ddMMMyyyy

Table 14.1.3 Patient Disposition (All Randomised Patients)

	50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Total (N=xx)
Full Analysis Set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Safety Set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PP Set	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

The denominator for each percentage is the number of randomised patients in the column

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ABX464-004

ddMMMyyyy

Table 14.1.4 Demographic and Baseline Characteristics (Full Analysis Set)

		50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Total (N=xx)
Age (years)	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x
Sex	N	xx	xx	xx	xx
	Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race	N	xx	xx	xx	xx
	White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Black	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Height (cm)	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x
Weight (kg)	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x
BMI (kg/m^2)	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x

The denominator for each percentage is the number of non-missing observations within the column
Age was calculated using DOB and date of informed consent and presented as age at last birthday.

BMI is the patient's body weight in kilograms divided by the square of the patient's height in metres.

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Table 14.1.5.1 Medical/Surgical History (Full Analysis Set)

	50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Total (N=xx)
Any medical/surgical history	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc				

The denominator for each percentage is the number of patients within the column
Medical history refers to conditions which stopped prior to or at the screening visit

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This layout also applies to:
Table 14.1.5.2 Current Medical Conditions (Full Analysis Set)

ABX464-004 ddMMMyyyy

Table 14.2.1.1.1 Time to Viral Rebound Analysis (Full Analysis Set)

		50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	p-value
Time to Viral Rebound (days)	N	xx	xx	xx	
	Mean	xx.xx	xx.xx	xx.xx	
	SD	xx.xx	xx.xx	xx.xx	
	Median	xx.xx	xx.xx	xx.xx	
	Minimum	xx.x	xx.x	xx.x	
	Maximum	xx.x	xx.x	xx.x	
Kaplan-Meier estimate (days)	Median (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
Log-Rank Test					x.xxxx

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This layout also applies to:
Table 14.2.1.1.2 Time to Viral Rebound Analysis (PP Set)
Table 14.2.1.2.1 Time to Virological Failure Analysis (Full Analysis Set)
Table 14.2.1.2.2 Time to Virological Failure Analysis (PP Set)

Programming note: log rank test is between 150mg dose and placebo only

ABX464-004 ddMMMyyyy

Table 14.2.2.1.1 Viral Load Analysis (Full Analysis Set)

		50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Estimated treatment effect ratio ABX-464/Placebo (95% confidence interval)	ANOVA p-value
Day 0	N	xx	xx	xx		
	Mean	xx.xx	xx.xx	xx.xx		
	SD	xx.xx	xx.xx	xx.xx		
	Median	xx.xx	xx.xx	xx.xx		
	Minimum	xx.x	xx.x	xx.x		
	Maximum	xx.x	xx.x	xx.x		
	LS Mean	xx.x	xx.x	xx.x	xx.x (xx.x, xx.x)	x.xxxx
Day 7	N	xx	xx	xx		
	Mean	xx.xx	xx.xx	xx.xx		
	SD	xx.xx	xx.xx	xx.xx		
	Median	xx.xx	xx.xx	xx.xx		
	Minimum	xx.x	xx.x	xx.x		
	Maximum	xx.x	xx.x	xx.x		
	LS Mean	xx.x	xx.x	xx.x	xx.x (xx.x, xx.x)	x.xxxx

Etc

ANOVA model is fitted with treatment as a fixed effect and analysis is conducted between 150mg dose and placebo only.

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This layout also applies to:
Table 14.2.2.1.2 Viral Load Analysis on Logarithmic Scale (Full Analysis Set)

Table 14.2.2.2 CD4+ T Cell Count Analysis (Full Analysis Set)
Table 14.2.2.3 CD4+/CD8+ T Cell Count Ratio Analysis (Full Analysis Set)

Programming note: analysis is between 150mg dose and placebo only

ABX464-004 ddMMMyyyy

Table 14.2.2.1.3 Time to Viral Load Control (Full Analysis Set)

		50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)
Time to Viral Load Control (days)	N	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x

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ABX464-004 ddMMMyyyy

Table 14.2.2.4.1 Total HIV DNA (Full Analysis Set)

		ABX-464			
		50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Pooled dose (N=xx)	Placebo (N=xx)
Day 0	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x
Day 28	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x
ART reintroduction visit	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x

'Pooled dose' is made up of patients on the 50mg ABX-464 and 150mg ABX-464 dose regimen

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ABX464-004 ddMMMyyyy

Table 14.2.2.4.2 Mean Change in Total HIV DNA: Day 0 vs Day 28 (Full Analysis Set)

		ABX-464			
		50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Pooled dose (N=xx)	Placebo (N=xx)
Mean change from Day 0 to Day 28 (copies/million PBMC)	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x
Mean percentage change from Day 0 to Day 28 (% copies/million PBMC)	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x
Mean percentage change in log10 transformed total HIV DNA from Day 0 to Day 28	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x

'Pooled dose' is made up of patients on the 50mg ABX-464 and 150mg ABX-464 dose regimen

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This layout also applies to:
Table 14.2.2.4.3 Mean Change in Total HIV DNA: Day 28 vs ART reintroduction (Full Analysis Set)

ABX464-004 ddMMMyyyy

Table 14.2.2.4.4 Total HIV DNA Analysis (Full Analysis Set)

		50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Binomial proportion difference* (95% confidence interval)	p-value
All patients at Day 28	N	xx	xx	xx		
	Responder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)		
	Non-responder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)		
					xx.x (xx.x, xx.x)	x.xxxx

*Binomial proportion difference is calculated as 150mg ABX-464 vs Placebo

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This layout also applies to:
Table 14.2.2.4.5 Total HIV DNA Analysis (PP Set)

ABX464-004 ddMMMyyyy

Table 14.3.1 Summary of Adverse Events (Safety Set)

	50mg ABX-464 (N=xx)		150mg ABX-464 (N=xx)		Placebo (N=xx)		Total (N=xx)	
	E	N (%)	E	N (%)	E	N (%)	E	N (%)
Any Adverse Event	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Any Treatment-Emergent Adverse Event	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Any Post-Treatment-Emergent Adverse Event	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Any Serious Adverse Event	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Any Severe Adverse Event	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Adverse Event leading to death	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)

The table presents number of events (E) and number and percentage of patients (N(%))
The denominator for each percentage is the number of patients within the column

Source: Listing 16.x.x
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ABX464-004 ddMMMyyyy

Table 14.3.2 Summary of Treatment-Emergent Adverse Events (Safety Set)

	50mg ABX-464 (N=xx)		150mg ABX-464 (N=xx)		Placebo (N=xx)		Total (N=xx)	
	E	N (%)	E	N (%)	E	N (%)	E	N (%)
Severe Treatment-Emergent Adverse Events	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Serious Treatment-Emergent Adverse Events	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Drug-Related Treatment-Emergent Adverse Events	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Serious Drug-Related Treatment-Emergent Adverse Events	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Treatment-Emergent Adverse Events leading to Study Drug Discontinuation	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)

The table presents number of events (E) and number and percentage of patients (N(%))
The denominator for each percentage is the number of patients within the column

Source: Listing 16.x.x
Path\Filename

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ABX464-004 ddMMMyyyy

Table 14.3.3.1 Treatment-Emergent Adverse Events, by SOC and PT (Safety Set)

	50mg ABX-464 (N=xx)		150mg ABX-464 (N=xx)		Placebo (N=xx)		Total (N=xx)	
	E	N (%)	E	N (%)	E	N (%)	E	N (%)
Any Treatment-Emergent Adverse Events	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
SOC	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
PT	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
PT	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Etc	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
SOC	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
PT	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
PT	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)
Etc	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)	xx	xx (xx.x%)

The table presents number of events (E) and number and percentage of patients (N(%))
The denominator for each percentage is the number of patients within the column

Source: Listing 16.x.x
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This layout also applies to:
Table 14.3.3.2 Severe Treatment-Emergent Adverse Events, by SOC and PT (Safety Set)
Table 14.3.3.3 Serious Treatment-Emergent Adverse Events, by SOC and PT (Safety Set)
Table 14.3.3.4 Drug-Related Treatment-Emergent Adverse Events, by SOC and PT (Safety Set)
Table 14.3.3.5 Serious Drug-Related Treatment-Emergent Adverse Events, by SOC and PT (Safety Set)
Table 14.3.3.6 Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation, by SOC and PT (Safety Set)

ABX464-004 ddMMMyyyy

Table 14.3.3.7 Mean Duration of Treatment-Emergent Adverse Events, by SOC and PT (Safety Set)

	50mg ABX-464 (N=xx)		150mg ABX-464 (N=xx)		Placebo (N=xx)		Total (N=xx)	
Duration (days)	E	Mean	E	Mean	E	Mean	E	Mean
SOC	xx	xx.xx	xx	xx.xx	xx	xx.xx	xx	xx.xx
PT	xx	xx.xx	xx	xx.xx	xx	xx.xx	xx	xx.xx
PT	xx	xx.xx	xx	xx.xx	xx	xx.xx	xx	xx.xx
Etc	xx	xx.xx	xx	xx.xx	xx	xx.xx	xx	xx.xx
	xx	xx.xx	xx	xx.xx	xx	xx.xx	xx	xx.xx
SOC	xx	xx.xx	xx	xx.xx	xx	xx.xx	xx	xx.xx
PT	xx	xx.xx	xx	xx.xx	xx	xx.xx	xx	xx.xx
PT	xx	xx.xx	xx	xx.xx	xx	xx.xx	xx	xx.xx
Etc	xx	xx.xx	xx	xx.xx	xx	xx.xx	xx	xx.xx

The table presents number of events (E) and mean duration of adverse event (days)

Source: Listing 16.x.x
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ABX464-004 ddMMMyyyy

Table 14.3.4.1 Summary of Haematology Parameters (Safety Set)

		50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Total (N=xx)
Haematocrit					
Baseline	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x
Day 7					
Etc					
Etc					

Source: Listing 16.x.x
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Programming note: start each parameter on a new page

This layout also applies to:
Table 14.3.4.2 Summary of Biochemistry Parameters (Safety Set)
Table 14.3.4.3 Summary of Urinalysis Parameters (Safety Set)

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ddMMMyyyy

Table 14.3.5.1 Shift Table of Haematology Parameters (Safety Set)

	50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Total (N=xx)
	Baseline	Baseline	Baseline	Baseline
	Normal Abnormal NCS Abnormal CS	Normal Abnormal NCS Abnormal CS	Normal Abnormal NCS Abnormal CS	Normal Abnormal NCS Abnormal CS
Haematocrit				
Day 7				
Normal	xx (xx.x%) xx (xx.x%) xx (xx.x%)	xx (xx.x%) xx (xx.x%) xx (xx.x%)	xx (xx.x%) xx (xx.x%) xx (xx.x%)	xx (xx.x%) xx (xx.x%) xx (xx.x%)
Abnormal NCS	xx (xx.x%) xx (xx.x%) xx (xx.x%)	xx (xx.x%) xx (xx.x%) xx (xx.x%)	xx (xx.x%) xx (xx.x%) xx (xx.x%)	xx (xx.x%) xx (xx.x%) xx (xx.x%)
Abnormal CS	xx (xx.x%) xx (xx.x%) xx (xx.x%)	xx (xx.x%) xx (xx.x%) xx (xx.x%)	xx (xx.x%) xx (xx.x%) xx (xx.x%)	xx (xx.x%) xx (xx.x%) xx (xx.x%)
Day 14				
Etc				
Etc				

CS=Clinically Significant; NCS=Non Clinically Significant

The denominator for each percentage is the number of non-missing observations within the column
Baseline is defined as the last non-missing value before the first dose of study drug.

Source: Listing 16.x.x
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This layout also applies to:
Table 14.3.5.2 Shift Table of Biochemistry Parameters (Safety Set)
Table 14.3.5.3 Shift Table of Urinalysis Parameters (Safety Set)
Table 14.3.7.2 Shift Table of 12-Lead Electrocardiogram (Safety Set)

Table 14.3.6 Vital Signs (Safety Set)

		50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Total (N=xx)
Systolic BP (mmHg)					
Baseline	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x
Day 7					
Etc					
Diastolic BP (mmHg)					
Heart Rate (bpm)					
Body temperature (°C)					
Weight (kg)					
BMI (kg/m^2)					

Source: Listing 16.x.x
Path\Filename

ABX464-004 ddMMMyyyy

Table 14.3.7.1 12-Lead Electrocardiogram (Safety Set)

		50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Total (N=xx)
Baseline	N	xx	xx	xx	xx
	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Abnormal CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Day 7					
Etc					

Source: Listing 16.x.x

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ddMMMyyyy

Table 14.3.8 Study Drug Exposure and Compliance (Full Analysis Set)

		50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Total (N=xx)
Number of administered doses	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x
Study drug exposure (days)	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	Etc				
Compliance (%)	N	xx	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx	xx.xx
	Etc				

Source: Listing 16.x.x

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ABX464-004 ddMMMyyyy

Table 14.3.9.1 Prior Medications (Full Analysis Set)

	50mg ABX-464 (N=xx)	150mg ABX-464 (N=xx)	Placebo (N=xx)	Total (N=xx)
Any prior medication[1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X, xxxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X0N, xxxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X0NXX, xxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
xxxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X0NXX, xxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
xxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X0N, xxxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X0NXX, xxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
xxxxxxxxxxxx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Etc				
Etc				

[1] Medication that stopped prior to date of first dose
WHO-DDE version <XX.X>
The denominator for each percentage is the number of patients in the safety set within the column

Source: Listing 16.x.x
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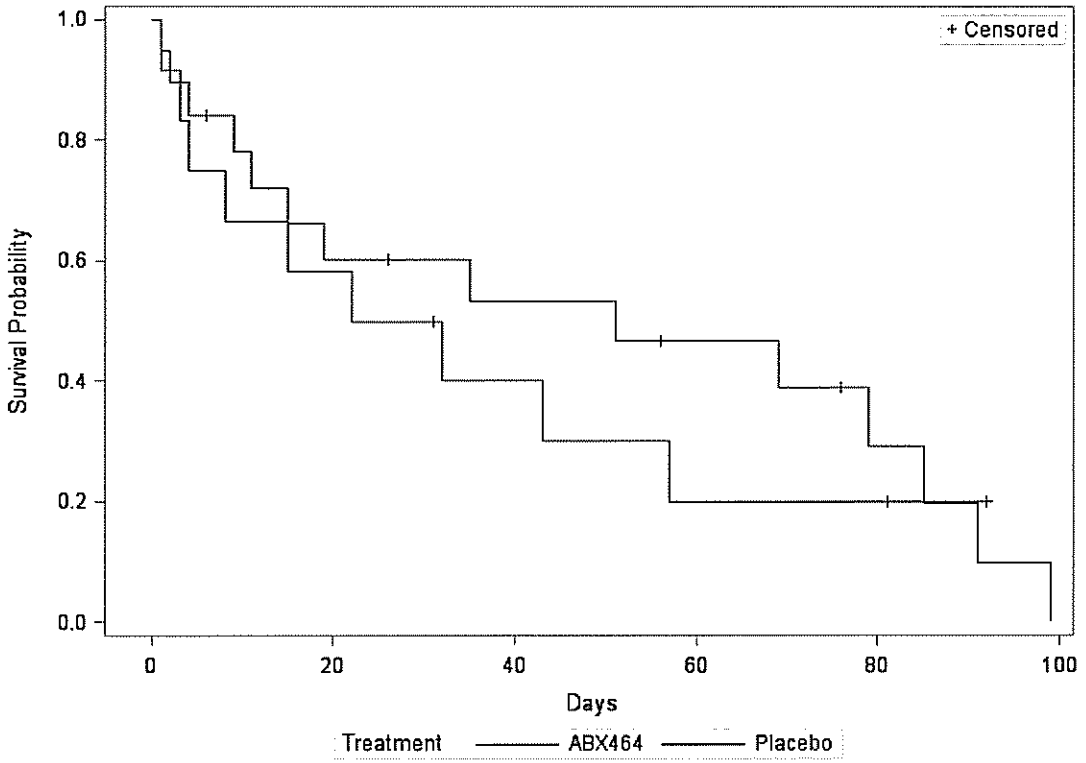
This layout also applies to:
Table 14.3.9.2 Maintained Medications (Full Analysis Set)
Table 14.3.9.3 Concomitant Medications (Full Analysis Set)

Figure 1 Kaplan-Meier Plot of Time to Viral Rebound (Full Analysis Set)



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This layout also applies to:
Figure 2 Kaplan-Meier Plot of Time to Virological Failure (Full Analysis Set)

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Listing 16.2.1 Discontinued Patients and Reason for Withdrawal

Treatment	Centre/ Patient number	First dose date	Last dose date	Date of withdrawal	Main reason for withdrawal
xxxxxx	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xxxxxxxxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xxxxxxxxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xxxxxxxxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xxxxxxxxxxxxxxxxxxxxxxxxxx
Etc					

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ABX464-004 ddMMMyyyy

Listing 16.2.2 Protocol Deviations

Treatment	Centre/ Patient number	Major deviation	Protocol deviation
xxxxxx	xxx-xxxx	Yes/No	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	Yes/No	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	Yes/No	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	Yes/No	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

Etc

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Listing 16.2.3 Analysis Datasets

Treatment	Centre/ Patient number	Full Analysis Set	Per Protocol Analysis Set	Safety Set
xxxxxx	xxx-xxxx	Yes/No	Yes/No	Yes/No
	xxx-xxxx	Yes/No	Yes/No	Yes/No
	xxx-xxxx	Yes/No	Yes/No	Yes/No
	xxx-xxxx	Yes/No	Yes/No	Yes/No

Etc

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Listing 16.2.4 Demographic Data

Treatment	Centre/ Patient number	Date of screening	Date of birth	Age (years)	Gender	Race	Weight (kg)	Height (cm)	BMI (kg/m^2)
xxxxxx	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xxxx	xxxx	xx.x	xxx.x	xx.x
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xxxx	xxxx	xx.x	xxx.x	xx.x
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xxxx	xxxx	xx.x	xxx.x	xx.x
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xxxx	xxxx	xx.x	xxx.x	xx.x
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xxxx	xxxx	xx.x	xxx.x	xx.x

Etc

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ABX464-004 ddMMMyyyy

Listing 16.2.5 Study Drug Exposure and Compliance

Treatment	Centre/ Patient number	Date of first dose	Date of last dose	Duration of exposure (days)	Number of administered doses	Scheduled number of doses	Compliance (%)
xxxxxx	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xx	xx	xx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xx	xx	xx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xx	xx	xx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xx	xx	xx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xx	xx	xx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xx	xx	xx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	xx	xx		
	Etc						
Etc							

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ABX464-004 ddMMMyyyy

Listing 16.2.6 Primary Endpoint Efficacy

Treatment	Centre/ Patient number	Date of last dose	Date of viral rebound	Date of virological failure	Time to viral rebound (days)	Time to virological failure (days)
xxxxxx	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xx	xx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xx	xx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xx	xx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	xx	xx
Etc						

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Listing 16.2.7 Adverse Event Listing

Treatment	Centre/ Patient number	Adverse Event Preferred Term SOC Term	Date of onset	Resolution date /ongoing	Duration of adverse event (days)	Outcome	Serious	Severity	Relationship to study drug	Action taken	Action taken with study drug
xxxxxxx	xxx-xxxx	xxxxxxxxx xxxxxxxx xxxxxxx	ddMMMyyyy	ddMMMyyyy	xx	Resolved /Etc	Yes /No	Mild /Moderate /etc	Not related /Related	None /Concomitant medication /Other	None /Discontinued /Etc
		xxxxxxxxx xxxxxxxx xxxxxxx	ddMMMyyyy	ddMMMyyyy	xx	Resolved /Etc	Yes /No	Mild /Moderate /etc	Not related /Related	None /Concomitant medication /Other	None /Discontinued /Etc
		Etc									
Etc											

ABX464-004 ddMMMyyyy

Listing 16.2.8.1 Laboratory Measurements: Haematology

Parameter	Treatment	Centre/ Patient number	Visit	Result	Unit	Reference range	Clinical significance
Haemoglobin	xxxxxxx	xxx-xxxx	Screening	xxx.xx	xxxx	xxx.xx, xxx.xx	Normal/ Abnormal CS/ Abnormal NCS
			Day 0	xxx.xx	xxxx	xxx.xx, xxx.xx	Normal/ Abnormal CS/ Abnormal NCS
			Day 7*	xxx.xx	xxxx	xxx.xx, xxx.xx	Normal/ Abnormal CS/ Abnormal NCS
			Etc	xxx.xx	xxxx	xxx.xx, xxx.xx	Normal/ Abnormal CS/ Abnormal NCS
		xxx-xxxx	Screening	xxx.xx	xxxx	xxx.xx, xxx.xx	Normal/ Abnormal CS/ Abnormal NCS
			Etc				
		Etc					
	Etc						
Etc							

*Outside the visit window

CS=Clinically Significant; NCS=Non Clinically Significant

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This layout also applies to:

Listing 16.2.8.2 Laboratory Measurements: Biochemistry

Listing 16.2.8.3 Laboratory Measurements: Urinalysis Programming note: remove reference range column for urinalysis listing

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Listing 16.4.1 Final Status

Treatment	Centre/ Patient number	First dose date	Last dose date	Completed treatment	Primary reason for discontinuation	Secondary reason for discontinuation
xxxxxx	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	Yes/No	xxxxxxxxxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	Yes/No	xxxxxxxxxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	Yes/No	xxxxxxxxxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxx
	xxx-xxxx	ddMMMyyyy	ddMMMyyyy	Yes/No	xxxxxxxxxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxx

Etc

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ABX464-004 ddMMMyyyy

Listing 16.4.2 Patient Visit Dates

Treatment	Centre/ Patient number	Visit	Date
xxxxxx	xxx-xxxx	xx	ddMMMyyyy
		xx	ddMMMyyyy
		xx*	ddMMMyyyy
		xx	ddMMMyyyy
Etc			

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Listing 16.4.3.1 Inclusion Criteria

Protocol versions: XXXX

	Definition of criterion
1	xxx
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

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Note: The list of criteria will be presented on the first page of the listing. Patient data will start on page 2.

Programming note: Repeat for each protocol amendment if the criteria change

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Listing 16.4.3.1 Inclusion Criteria

Treatment	Centre/	Protocol	Criteria											
	Patient number	version	1	2	3	4	5	6	7	8	9	10	11	12
xxxxxx	xxx-xxxx	x.xx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
	xxx-xxxx	x.xx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
	xxx-xxxx	x.xx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
	xxx-xxxx	x.xx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
Etc														

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This layout also applies to:

Listing 16.4.3.2 Exclusion Criteria

Listing 16.4.4 Medical History

Treatment	Centre/ Patient number	Condition SOC PT	Date of diagnosis	Ongoing/ End date	Medication taken/ Treatment given?	Related therapy number
xxxxxx	xxx-xxxx	xxxxxxxxxxxxx xxxxxxxxxxx xxxxxxxxxx	ddMMMyyyy	Yes/ No (ddMMMyyyy)	Yes/No	xx
		xxxxxxxxxxxxx xxxxxxxxxxx xxxxxxxxxx	ddMMMyyyy	Yes/ No (ddMMMyyyy)	Yes/No	xx
		xxxxxxxxxxxxx xxxxxxxxxxx xxxxxxxxxx	ddMMMyyyy	Yes/ No (ddMMMyyyy)	Yes/No	xx

Etc

ABX464-004 ddMMMyyyy

Listing 16.4.5 Raw Efficacy Scores

Treatment	Centre/ Patient number	Visit	Viral Load	CD4+ T Cell Count	CD8+ T Cell Count	CD4+/CD8+ T Cell Count Ratio	HIV Reservoir
xxxxxx	xxx-xxxx	xx	xx	xx	xx	xx	xx
		xx	xx	xx	xx	xx	xx
		xx	xx	xx	xx	xx	xx
		xx*	xx	xx	xx	xx	xx

Etc

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ABX464-004 ddMMMyyyy

Listing 16.4.6 Vital Signs

Treatment	Centre/ Patient number	Visit	Date of visit	Systolic BP (mmHg)	Diastolic BP (mmHg)	Heart rate (beats/min)	Body temperature (°C)	Weight (kg)	BMI (kg/m²)
xxxxxx	xxx-xxxx	xx	ddMMMyyyy	xxx	xxx	xxx	xx.x	xx.x	xx.x
		xx	ddMMMyyyy	xxx	xxx	xxx	xx.x	xx.x	xx.x
		xx*	ddMMMyyyy	xxx	xxx	xxx	xx.x	xx.x	xx.x
		xx	ddMMMyyyy	xxx	xxx	xxx	xx.x	xx.x	xx.x

Etc

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ABX464-004 ddMMMyyyy

Listing 16.4.7 Physical Examination

Treatment	Centre/ Patient number	Visit	Date of Visit	Body system	Status	Abnormality
xxxxxx	xxx-xxxx	Screening	ddMMMyyyy	Eyes	Normal/ Abnormal NCS/ Abnormal CS/ Not done	xxxxxxxxxxxxxxxxxxxxxxxxxx
				Ear/Nose/Throat	Normal/ Abnormal NCS/ Abnormal CS/ Not done	xxxxxxxxxxxxxxxxxxxxxxxxxx
				Lungs/Thorax	Normal/ Abnormal NCS/ Abnormal CS/ Not done	xxxxxxxxxxxxxxxxxxxxxxxxxx
				Heart/ Cardiovascular system	Normal/ Abnormal NCS/ Abnormal CS/ Not done	xxxxxxxxxxxxxxxxxxxxxxxxxx
				Etc		
		xx*	ddMMMyyyy	Eyes	Normal/ Abnormal NCS/ Abnormal CS/ Not done	xxxxxxxxxxxxxxxxxxxxxxxxxx
				Etc		
Etc						

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ABX464-004 ddMMMyyyy

Listing 16.4.8 12-Lead Electrocardiogram

Treatment	Centre/ Patient number	Visit	Date of visit	Time	Investigator's interpretation	Abnormality
xxxxxx	xxx-xxxx	Day 0	ddMMMyyyy	hh:mm	Normal/ Abnormal NCS/ Abnormal CS	xxxxxxxxxx
		Day 7	ddMMMyyyy	hh:mm	Normal/ Abnormal NCS/ Abnormal CS	xxxxxxxxxx
		Day 28*	ddMMMyyyy	hh:mm	Normal/ Abnormal NCS/ Abnormal CS	xxxxxxxxxx
		Etc				
	Etc					
Etc						

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Listing 16.4.9.1 Prior Medications

Treatment	Centre/ Patient number	Therapy ATC Code PT	Indication	Dose	Unit	Frequency	Route	Start date (Stop date)	Given for Procedure/ Non-Drug Therapy? (Related procedure number)
xxxxxx	xxx-xxxx	xxxxxxxxxxxxxxx xxxxxxxxxxxxx xxxxxxxxxxx	xxxxxxx	xx.x	xxx	xxx	xxx	ddMMMyyyy (ddMMMyyyy)	Yes (xxx) / No
		xxxxxxxxxxxxxxx xxxxxxxxxxxxx xxxxxxxxxxx	xxxxxxx	xx.x	xxx	xxx	xxx	ddMMMyyyy (ddMMMyyyy)	Yes (xxx) / No
		xxxxxxxxxxxxxxx xxxxxxxxxxxxx xxxxxxxxxxx	xxxxxxx	xx.x	xxx	xxx	xxx	ddMMMyyyy (ddMMMyyyy)	Yes (xxx) / No

Etc

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This layout also applies to:

Listing 16.4.9.2 Maintained Medications (Programming note: can have stop date as 'ongoing')

Listing 16.4.9.3 Concomitant Medications (Programming note: can have stop date as 'ongoing')

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Listing 16.4.10 Procedures/ Non-Drug Therapies

Treatment	Centre/ Patient number	Procedure /Therapy	Start date	Ongoing / End date	Given for pre-existing condition? (Related medical history number)	Given for adverse event? (Related adverse event number)
xxxxxx	xxx-xxxx	xxxxxxxxxxxxxx	ddMMMyyyy	Yes / No (ddMMMyyyy)	Yes (xxx) / No	Yes (xxx) / No
		xxxxxxxxxxxxxx	ddMMMyyyy	Yes / No (ddMMMyyyy)	Yes (xxx) / No	Yes (xxx) / No
		xxxxxxxxxxxxxx	ddMMMyyyy	Yes / No (ddMMMyyyy)	Yes (xxx) / No	Yes (xxx) / No

Etc

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ABX464-004 ddMMMyyyy

Listing 16.4.11 Serology

Treatment	Centre/ Patient number	HBV		HCV		HIV	
		Sampling date	Result	Sampling date	Result	Sampling date	Result
xxxxxx	xxx-xxxx	ddMMMyyyy	Positive/ Negative/ Indeterminate/ Not done	ddMMMyyyy	Positive/ Negative/ Indeterminate/ Not done	ddMMMyyyy	Positive/ Negative/ Indeterminate/ Not done
	xxx-xxxx	ddMMMyyyy	Positive/ Negative/ Indeterminate/ Not done	ddMMMyyyy	Positive/ Negative/ Indeterminate/ Not done	ddMMMyyyy	Positive/ Negative/ Indeterminate/ Not done
	xxx-xxxx	ddMMMyyyy	Positive/ Negative/ Indeterminate/ Not done	ddMMMyyyy	Positive/ Negative/ Indeterminate/ Not done	ddMMMyyyy	Positive/ Negative/ Indeterminate/ Not done
	Etc						
Etc							

*Outside the visit window

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ABX464-004 ddMMMyyyy

Listing 16.4.12 Blood and Serum Pregnancy Test

Treatment	Centre/ Patient number	Visit	Test done	Reason not done	Date of test	Result	
						Blood test	Serum test
xxxxxx	xxx-xxxx	Screening	Yes/No/Not applicable	xxxxxxxxxxxx	ddMMMyyyy	Positive/ Negative	
		xx	Yes/No/Not applicable	xxxxxxxxxxxx	ddMMMyyyy		Positive/ Negative
		xx*	Yes/No/Not applicable	xxxxxxxxxxxx	ddMMMyyyy		Positive/ Negative
		xx	Yes/No/Not applicable	xxxxxxxxxxxx	ddMMMyyyy		Positive/ Negative
		Etc					
Etc							

*Outside the visit window

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Programming note: blood test column should only be populated for screening visit results

16 APPENDICES

16.1 STUDY FLOWCHART

	Screening	Days						Treatment interruption - Follow-up			
Time Window		± 2 days (except D25 ± 4)						± 2 days			
Days	D-21	D0	D7	D14	D21	D25	D28	Twice weekly for 3 weeks	Every week till VR	ARTs reintroduction visit	FU visit(s)***
Obtained Informed Consent	X										
Check of IN/EX Criteria	X	X									
Physical Examination	X	X	X	X	X	X	X		X	X	X
Body Weight (kg)	X	X	X	X	X	X	X		X	X	X
Height Measurement (cm)	X										
Medical History	X										
Medical Calls to patients		Day 3 & 5									
Serology: HBV, HCV, HIV	X										
Hematology + Biochemistry	X	X	X	X	X	X	X		X	X	X*****
CD4 and CD8 count	X	X	X	X	X	X	X	X	X	X	X
Urinalysis	X	X	X	X	X	X	X	X****	X	X	
Blood Pregnancy test	X										
Urine pregnancy test	X	X	X	X	X	X	X		X	X	
Vital signs	X	X	X	X	X	X	X		X	X	
ECG (12 lead)	X	X	X				X			X	
DRV/RTV-COBI prescription	X	X	X	X	X	X	X			X	X
ABX464/placebo treatment dispensation and patient diary review		X	X	X	X	X	X				
Blood samples		X*	X*	X*	X*	X**					

drug pK											
Blood samples for viral load /miRNA	X	X	X	X	X	X	X	X	X	X	X
Genotyping										X	
Leukopheresis (optional)	X									X	
Blood samples for reservoir assessment • Viral DNA • TILDA	X	X					X			X X	
Adverse Events recording		X	X	X	X	X	X		X	X	X

* pre DRV/RTV or DRV/COBI morning dose

** pre DRV/RTV or DRV/COBI morning dose, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 12 and 24 h post-dose (hospitalization is not required)

*** Every 14 days till undetectable VL

**** urinalysis to be performed once a week

***** only biochemistry required and for at least 28 days after treatment interruption