ACTG A5353

A Study to Evaluate Dolutegravir plus Lamivudine Dual Therapy for the Treatment of Naïve HIV-1-infected Participants

Statistical Analysis Plan – Final

Version 1.0

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This is SAP Version 1.0 with names of authors, names of publication writing team members, and analysis timeline redacted.

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1 Introduction

This document describes the proposed content for the primary statistical analysis of ACTG A5353. This document focuses on analyses that address the key safety and efficacy outcome measures, including those needed to address the study's primary and secondary objectives. A subset of these analyses will form the basis of reports provided to the ACTG Study Monitoring Committee (SMC) while the study is ongoing. This analysis plan thus includes the key analyses which might lead to modification or termination of the study, and hence also form the core of any presentation or publication used to disseminate the primary conclusions of the study. It is, however, recognized that this analysis plan may be modified by the study team as new information becomes available outside of the study, or to reflect recommendations made by the SMC. In addition, some analyses, tables, or figures may be omitted at interim analyses if there are insufficient data to warrant analysis or at the request of the SMC.

2 Study schema, hypotheses and objectives

2.1 Study schema

DESIGN	This is a phase II, single-arm, open-label, pilot study of dolutegravir (DTG) plus lamivudine (3TC). All participants will undergo routine monitoring including plasma HIV-1 RNA levels, CD4+ cell count, hematology, chemistry, and urinalysis. Population-based protease (PR), reverse transcriptase (RT), and integrase genotyping will be done at the time of confirmed virologic failure. Plasma samples will be stored for potential future studies to assess the impact of adherence, drug-resistant minority viral variants, and DTG exposure on virologic and CD4+ cell count responses to DTG plus 3TC. All participants will also undergo UGT1A1 genotyping.
DURATION	52 weeks
SAMPLE SIZE	120 participants
POPULATION	HIV-1 infected, antiretroviral (ARV) naïve men and women, 18 years and older, with plasma HIV-1 RNA ≥1,000 copies/mL and <500,000 copies/mL, and with no evidence of a major PR mutation, any RT or any integrase mutations as defined by the 2014 International Antiviral Society (IAS)-USA drug resistance mutations list. At least 25% (N=30) of the participants will have screening HIV-1 RNA >100,000 copies/mL. The study will aim to enroll ≥20% women.
REGIMEN	DTG 50 mg once a day (QD) plus 3TC 300 mg QD for 52 weeks

2.2 Hypothesis

In treatment-naive participants, dual therapy with DTG plus 3TC is efficacious and well tolerated.

2.3 Primary Objective

To estimate the virologic success rate at week 24 after initiating DTG plus 3TC.

2.4 Secondary Objectives

- To compare the efficacy of DTG plus 3TC in participants with baseline HIV-1 RNA ≤ 100,000 versus > 100,000 copies/mL.
- To estimate the virologic success rate of DTG plus 3TC therapy at weeks 12 and 48.
- To describe emergent integrase and RT resistance in participants with virologic failure.
- To evaluate the safety and tolerability of DTG plus 3TC.
- To evaluate changes in CD4+ cell counts and serum lipids.
- To store plasma samples for future studies of the impact of drug-resistant minority viral variants on response to DTG plus 3TC.
- To describe the relationships between functional genetic variants in selected *UGT1A1* and other human genes relevant to the study drugs and responses (virologic and immunologic) as well as adverse events observed with DTG plus 3TC.
- To store random-timed plasma samples that may be used to characterize associations between plasma DTG exposure, adherence, responses (virologic and immunologic) as well as adverse events observed with DTG plus 3TC.

3 General analysis considerations

Unless otherwise specified, data will be summarized **overall and by screening HIV-1 RNA strata (≤ 100,000 vs. > 100,000 copies/mL).** Throughout this document, "study entry" is defined as the visit date of a participant's entry visit captured on the study initiation case report form (ADM0010). Annotations in square brackets ([xxx]) will provide the source table/view names and in cases, target fields.

3.1 Timing of Primary Analyses

The primary efficacy outcome measure is at week 24 while the study follow-up is week 52. Primary analysis will be conducted after all participants complete required follow-up for evaluation of primary efficacy outcome measure at week 24. Secondary analysis will commerce after all participants complete week 52 follow-up.

3.2 Study visit windows

For longitudinal outcomes, with the exception of the week 2 visit, analysis windows around each study visit will be defined as non-overlapping intervals spanning the entire period of follow-up starting and ending half-way between each successive study visit at which a given evaluation is expected. For example, for clinic visits and HIV-1 RNA evaluations, the week 12 window will span the period from >10 to 14 weeks after enrollment, the week 24 visit window will span the period from >22 to 28 weeks, etc. The exception with respect to the week 2 visit window is that this visit window will span the entire period from after the start of treatment to week 3. In all cases, week 0 will include evaluations up to and including the date of study entry. The start time for calculation of study week will be the date of study entry (variable onstdt in status dataset).

3.3 Handling Multiple Observations

Unless otherwise specified, in the event of multiple evaluations in a visit window, the evaluation taken closest to the center of the week window (the actual scheduled study week) will be used.

Exception: multiple HIV-1 RNA evaluations in week 24 and 48 windows will be handled as per section 10.

3.4 Listings of Data in Reports

Listings of data by individual study participants are described below to facilitate the interpretation of the study results. To help protect confidentiality of data, the content of these lists will be limited and will not include dates, participants' ACTG identifier numbers or other combinations of information that might identify an individual participant (except that these may be included in the confidential closed reports prepared for SMC review).

3.5 Definition of Baseline

Baseline observations are defined as the last observations prior to the date of first dose of study treatment, unless otherwise specified in the protocol.

3.6 Period of Follow-up

Per protocol section 6.2.3, week 24 evaluation and confirmation evaluation, if warranted, will serve as the evaluations for the study's primary endpoint. Study follow-up will continue until the week 52 evaluation to complete study evaluation for secondary endpoints.

3.7 Validation of Programs

All programs creating treatment codes, derived datasets, formats, and primary analyses will be validated in accordance with SOP PROG.10066 and PROG.10067. All user options files will be validated in accordance with SOP PROG.10071.

The primary analyses will be additionally validated through independent coding.

4 Study population

4.1 Screening [Not for interim analysis]

Table: number (%) screened by site and month/year
Table: number (%) screened by screening HIV-1 RNA
Table: number (%) screened by sex
Table: number (%) screened by screening status (enrolled, not enrolled with detailed reason for not enrolled)

Note: clearly state in the report that there may be multiple screen number for any one participant and there may be more than one reason for any screen failure.

4.2 Accrual and eligibility violations

Table: number (%) enrolled by site and month/year
Table: number (%) enrolled by screening HIV-1 RNA
Table: number (%) enrolled by sex

Note: the dates of first and last enrollments will be provided in a footnote to the table.

List: Description of violations of eligibility criteria and details of exclusion from analyses, screening RNA category, site, and length of follow-up prior to exclusion due to violation [STATUS, ANSTAB].

Note: Participants who are registered and later found to be ineligible will be excluded from all analyses. Information on how long they have been followed on the study will be provided in the list.
Note: Participants who are registered but do not attend their entry visit (as determined from ADM0010 and ADM0050) will be excluded from all analyses.

4.3 Baseline characteristics

Purpose: to describe the characteristics (demographic, health status and other key characteristics) of enrolled participants at study entry.

Selected baseline characteristics will be analyzed as continuous, categorical, or both, as appropriate. Tables will provide the number of participants, number of missing data points, median (Q1-Q3), mean, standard deviation, P10 and P90, minimum and maximum for continuous variables (with transformations as appropriate) and number (%) for categorical variables. In the calculation of percentages, participants with missing data will not be included in the denominator.

All categorical variables will have missing categories if data for a particular participant is missing. **For interim analysis**, since data comes in at different speeds depending on the CRF, there will also be a category available showing that the form containing the specific data has not yet been entered. This category will be denoted “Missing Form”.

Demographic Information

a. Age on day of study entry (years): N, N missing, mean, standard deviation, median, 1st and 3rd quartiles, 10th and 90th percentiles, minimum and maximum; number (%) by age group (18-29, 30-39, 40-49, 50-59, 60+ years, rounded down) [PATIENT].
b. Sex: Number (%) by category (male/female) [PATIENT].
Note: Per protocol, the study aims to enroll at least 20% women.
c. Self-reported race/ethnicity: number (%) by category [PATIENT].

Health Status

a. Screening HIV-1 RNA level: number (%) by category (> 100,000 copies/mL or ≤ 100,000 copies/mL) [ANSTAB].
Note: Per protocol, the study aims to enroll at least 25% of participants with screening HIV-1 RNA > 100,000 copies/mL.
b. Baseline HIV-1 RNA level (copies/ml) and corresponding results for $\log_{10}$ copies/ml: N, median, 1st and 3rd quartiles, 10th and 90th percentiles, minimum and maximum; number (%) by category (<1,000, 1,000-9,999, 10,000-99,999, 100,000-200,000, >200,000) [RNALDMS].
Note: Baseline is the closest value prior to date of first dose of study treatment and after screening.
c. Baseline CD4+ count: N, N missing, mean, standard deviation, median, 1st and 3rd quartiles, 10th and 90th percentiles, minimum and maximum; number (%) by category (< 200, 200- 349, 350-499, 500-649, 650-799, ≥ 800) [LBW0054].
Note: Baseline is the closest value prior to date of first dose of study treatment and after screening.
d. Baseline CD8+ count: N, N missing, mean, standard deviation, median, 1st and 3rd quartiles, 10th and 90th percentiles [LBW0054].
Note: Baseline is the closest value prior to date of first dose of study treatment and after screening.
e. Baseline CD4:CD8 ratio: N, N missing, mean, standard deviation, median, 1st and 3rd quartiles, 10th and 90th percentiles, minimum and maximum.
f. IV drug use: number (%) by category (never, currently, previously) [CASE].
g. Hepatitis C status: number (%) by category (positive, negative, indeterminate) [SR0009].
h. PEP or PrEP history: number (%) by category (yes, no) [HXW0171].
i. Screening resistance genotype obtained: number (%) by category (yes, no) [LBW0115].

5 Study and treatment status

Purpose: To summarize the extent of follow-up and reasons for premature study treatment and study discontinuation

A CONSORT diagram will be provided at final analysis only summarizing key components of study follow-up and treatment status of participants, including number enrolled, starting treatment (with reasons why did not start treatment), complete study on study treatment, complete study off study treatment, off study prematurely with reason.

5.1 Study status

Table: number (%) of the following categories:

a. Complete study per protocol [STATUS]
b. On study with subcategories of < 24 weeks on study and ≥ 24 weeks on study (interim and primary analysis only) [STATUS]
c. Died [STATUS]
d. Prematurely discontinued study for reasons other than death (with subcategories showing reason using coded reason). The premature study discontinuation date will be date of last participant contact. [STATUS, F1601]

List of participants off study prematurely: site, week of study, screening RNA category, coded and specified reason, week of last clinic visit, week of last participant contact, and whether participants off study prior to reaching the study's primary endpoint (week 24) or virologic failure [STATUS, ADM0050, F1601].

Table: Time (weeks) from study entry to last visit at which contact with the participant was reported: mean, standard deviation, median, 10^{th} and 90^{th} percentiles, minimum, maximum [STATUS, ADM0050].

Note: A footnote to this table will provide number of participants for whom last visit with contact did not involve the participant attending a study clinic.

5.2 Currency of Follow-Up (Interim Only)

Table: Time (weeks) from last clinic visit to the date of data download: median, 1^{st} and 3^{rd} quartiles, 10^{th} and 90^{th} percentiles, minimum, maximum; and number (%) by category of 0-4, 4-8, 8-12, and >12 weeks [STATUS & AMD0050].

Note: Participants who have died or discontinued study follow-up will be excluded; the number of participants and length of time on study before death or discontinuation of study follow-up will be included in a footnote.

5.3 Treatment Status

Table: number (%) for categories as follows:

a. Completed study treatment per protocol [F1601/TXT0004/F4003]
b. On study treatment with subcategories of < 24 weeks on study treatment and ≥ 24 weeks on study treatment (interim and primary analysis only) [STATUS]
c. Prematurely discontinued study treatment (with subcategories showing reasons) [TXT0004/F4003]

Study treatment discontinuation is defined as permanent discontinuation of DTG or 3TC more than 14 days prior to protocol completion, death, premature study discontinuation, or the addition of an antiretroviral drug to the regimen for greater than one day. Analysis will be based on TXT0004 with cross-reference to F4003/F1601 as appropriate.

List of participants off study treatment prematurely: site, week of study treatment, coded and specified reason off study treatment [F4003, STATUS].

Table: Number (%) of days after study entry to study treatment initiation [STATUS].

List: Participants that initiated DTG + 3TC more than 3 days after study entry with length of time to treatment initiation and detailed reason for delay [ADM0020].

Table: Number (%) of treatment interruption (Yes/no) with subcategories of duration of treatment interruption (days, 3-<14, 14+) [TXT0004]

List: Participant-initiated and/or protocol-mandated treatment interruption for > 3 days detailed reason [TXT0004]

6 Pregnancy

List: Pregnancies, study week of pregnancy test (if available), study week of pregnancy outcome, pregnancy outcome, delivery circumstances, ART during the entire course of the pregnancy from pregnancy report to

two weeks after outcome, for live births: birth weight, gestational age by LMP, any congenital abnormalities [EVW0180].

7 Adherence to study treatment

Purpose: to summarize how compliant participants were with study treatment.

Table: percentage of missed dose based on 4-day recall [QL0757]: median, 1st and 3rd quartile, 10th and 90th percentiles, minimum, maximum. The percentage of missed dose is calculated across both study drugs as follows: (ds1ago1 + ds1ago2 + ds1ago3 +ds1ago4 + ds2ago1 + ds2ago2 + ds2ago3 +ds2ago4)/ ((dosnum1+dosnum2)*4).

Note: if answer to Question 1 is No, then the percentage of missed dose will not be calculated.

8 Data completeness

Purpose: to summarize how compliant participants were with visits, study-defined evaluations, and CRFs and laboratory data are being recorded in the database in a timely fashion. Data completeness will not be presented by stratum.

Table: Summary of missed visits and reasons for missed visits, if missing data is an issue.

Tables: Data availability for the following key study tests, measurements, and specimens: HIV-1 RNA [RNALDMS], CD4+ cell count [LBW0054], CD8+ cell count [LBW0054], self-reported adherence form completion [QL0757], whole blood storage for pharmacogenomics [L_ALIQ], stored plasma for minority viral variants [L_ALIQ], total fasting cholesterol [F2861], and serum creatinine [LBW0144]. The weeks at which each measurement is expected are detailed in the visit and evaluation schedule in section 3.4 above. Each table will include study week, participants expected to have data entered, observed visits among those expected, and the number of complete observations of the measurement of interest.

9 Safety

9.1 Adverse Event Reporting Requirements

Protocol section 6.3 states the following reporting requirements:

> Signs and Symptoms
>
> Grade ≥ 2 rash and all other grade ≥3, any signs and symptom lead to a change in treatment regardless of grade [EVW0314].
>
> Diagnoses
>
> All diagnoses identified by the ACTG criteria for clinical events and other diseases [EVW0314].
>
> Laboratory Evaluations
>
> Grade ≥ 3 or any laboratory toxicities that lead to a change in treatment, regardless of grade [EVW0314].
>
> Note: Creatinine and fasting lipid values are required to be reported regardless of grade are not considered adverse events unless they are Grade ≥ 3 or lead to a change in treatment.

9.2 Summaries of Post-Entry Adverse Events

Table: Summary of adverse events [EVW0314] presented by MedDRA preferred term (PT) according to primary system organ class (SOC) and grade giving the number (%) of participants reporting at least one event (PT) and the number (%) of participants reporting at least one event within each SOC. Participants will be counted only once (at the highest reported grade for the PT, SOC, and overall totals.

Table: Summary of adverse events [EVW0314] by type (sign/symptom, diagnosis, laboratory measurement, and death) giving the number (%) of participants within each category and overall.

List: Listing of all adverse events [EVW0314] by participant (publicid). The listing will detail the participant, scheduled study week of the event, the type of event (sign/symptom, diagnosis, laboratory measurement, and death), the specific name of the event, whether the event was resolved, the event grade, and whether the event was related to study treatment. Associated events will be indented to the associated primary events.

List: narrative of all deaths including weeks on study at time of death, week of last study evaluation, baseline and most recent HIV-1 RNA and CD4 count, weeks since the last dose of study treatment, weeks since the last dose of other ART treatment (if applicable), last ART regimen, and site's reports of primary cause of death (text, categorization and diagnosis), and site's determination of relatedness to study treatment.

10 Primary Outcome Measure

10.1 Virologic success at week 24

Primary efficacy outcome of the study is virologic success at week 24. Virologic success is defined as HIV-1 RNA < 50 copies/mL and on study treatment (FDA Snapshot definition: Human immunodeficiency virus-1 infection: developing antiretroviral drugs for treatment guidance for industry, November 2015).

The virologic success at week 24 will be tabulated as below:

Virologic Success	N (%)
HIV-1 RNA < 50 copies/mL	N
Virologic Non-success	N (%)
HIV-1 RNA ≥ 50 copies/mL	N
Discontinued study drug for lack of efficacy	N
Discontinued study drug for other reasons; HIV-1 RNA ≥ 50 copies/mL	N
Discontinued study drug for other reasons; HIV-1 RNA < 50 copies/mL	N
No Virologic Data at Week 24 window	N (%)
Discontinued study/study drug due to AE or Death	N
Discontinued study/study drug for Other Reasons	N
On study but missing data in window	N

Table: Primary outcome measure evaluability N(%): Evaluable vs. HIV-1 RNA pending. **[For interim analysis only]**

Table: Proportion of participants with virologic success and 95% CI.

Notes:

- The primary outcome window at week 24 is defined as week 22-28, i.e., 155-196 days, inclusive. The window is defined based on the guidance "Window size is one-half the duration of time between study visits".

- For interim analysis:

    - Evaluable participants are those with week 24 visit (ADM0020 visit form and/or HIV-1 RNA results in database) or those who discontinued the study prior to the visit window.

    - Participants with premature study discontinuation will be evaluated for primary outcome measure regardless whether their potential on-study follow-up would reach week 24 by data retrieval date.

- Snapshot analysis follows a Virology First hierarchy. Because this is primarily a virologic endpoint, the hierarchy for assessing row and column percentages is *HIV-1 RNA < 50 copies/mL* or *HIV RNA ≥ 50 copies/mL,* **first**, for any given window followed by reasons for *No Virologic Data in the window*.

- Data in the window
    - Virologic outcome should be determined by the last available measurement while the participant is on treatment and continued on study within the time window.
    - Participants who had changes in ART will be counted as virologic non-success.

- No data in the window
    - Discontinued study due to Adverse Event or Death.
        - Any participant who discontinues because of an AE or death **before** the window should be classified as *Discontinued due to AE or Death*, regardless of the HIV-1 RNA result, even if the HIV-1 RNA < 50 copies/mL at the time of discontinuation.
        - If a participant has an HIV-1 RNA in the time window and also discontinues after the viral load was tested **in the time window**, the viral load data should be used to classify the participant's response.
    - Discontinued study for Other Reasons
        - If a participant discontinues the study before the window because of lack of efficacy then the participant should be included in *the HIV-1 RNA ≥ 50 copies/mL* row and not in the *Discontinued for Other Reasons* row.
        - For participants who discontinued for Other Reasons, it is important to realize that in the Virology First hierarchy only participants who have achieved virologic suppression can be counted as *Discontinued for Other Reasons*. Example, if a participant discontinues because of the withdrew of consent and the HIV-1 RNA at the time of discontinuation was ≥ 50 copies/mL, then s/he should be categorized as *HIV RNA ≥ 50 copies/mL* and not *Discontinued for Other Reasons.*
    - On study but missing data in window
        - Only participants remaining on study but with missing virologic data should be classified as this category.

- Dataset for Snapshot approach should contain, at minimum, the following information:
    - PATID

- Study day and date of last study treatment
- Virologic outcome based on the Snapshot approach (i.e., *HIV-1 RNA < 50 copies/mL, HIV-1 RNA ≥ 50 copies/mL, Discontinued due to AE or death, Discontinued for Other Reasons, On study but missing data during window*)
- HIV-1 RNA measurement and the corresponding study day and date used to determine the above virologic outcome if the measurement was not missing
- Study day and date when the participant switched to non-study treatment because of lack or loss of virologic suppression (VF), if applicable
- Study day and date for permanent study discontinuation, reason for discontinuation, and last on study treatment HIV-1 RNA measurement before discontinuation for the participants who discontinued study treatment

11 Secondary Outcome Measures

11.1 Comparison of efficacy in participants with baseline HIV-1 RNA ≤ 100,000 vs. > 100,000 copies/mL

Proportion of participants with virologic success at week 24 between participants with baseline HIV-1 RNA ≤ 100,000 vs. > 100,000 copies/mL will be compared using Fisher's exact test.

11.2 Virologic success at weeks 12 and 48 [Not done for interim analysis]

The analysis of virologic success at weeks 12 and 48 will follow the same approach for virologic success at week 24 (section 12.1).

Notes:

- The outcome window at week 12 is defined as week 10-14, i.e., 71-98 days.
- The outcome window at week 48 is defined as week 44-52, i.e., 309-364 days. Since week 52 is the final study visit, the window will be the latter of (last day of study follow-up and 364 days).

11.3 Virologic failure

Virologic failure is defined as follows (in protocol section 6.2.3):

- Weeks 16 or 20:
  - confirmed plasma HIV-1 RNA > 400 copies/mL
- Week 24 or later:
  - confirmed plasma HIV-1 RNA > 200 copies/mL

Notes:

- Participants are evaluated for virologic failure regardless of whether on study treatment.
- Confirmation will be determined based on any two consecutive evaluations meeting the virologic failure definition regardless of the time between them.
- Participants discontinuing the study (for any reason, including death and lost to follow-up) will be considered a virologic failure if their last measurement meets the definition of virologic failure but no confirmatory measurement was obtained. All other participants' follow-up will be censored immediately after the last available plasma HIV-1 RNA measurement.

Table: N (%) of virologic failures and by subcategories of prior to week 16, after week 16 and prior to week 24, and after week 24.

Table: Frequency of days from date of initial VF measurement to date of confirmation measurement (< 7 days, ≥7-≤28 days, > 28 days, lost to follow-up)

Table: Kaplan-Meier estimates of the cumulative probability of VF overall with 95% confidence intervals estimated with Greenwood's variance at weeks 24 and 48.

Figure: Kaplan-Meier curve

11.4 Plasma HIV-1 RNA level < 50 and < 200 copies/mL

Three analyses will be performed with alternative considerations of missing data, treatment discontinuation and loss to follow-up:

- ITT, pure virologic missing=ignored. The numerator will include participants with HIV-1 RNA < 50 (200) copies/mL; the denominator will include all participants with an HIV-1 RNA evaluation at the given week.
- ITT missing/off study/off treatment=failure. The numerator will include participant with HIV-1 RNA < 50 (200) copies/mL and still on initial treatment; the denominator will include all participants with potential for the given week of follow-up based on the date of registration.
- AT, purely virologic missing=ignored. The numerator will include participants with HIV-1 RNA < 50 (200) copies/mL and still on initial treatment; the denominator will include participants on initial treatment with an HIV-1 RNA evaluation at the given week.

Note: at interim analyses, only ITT, pure virologic missing=ignored approach will be used.

Table: proportions of participants with HIV-1 RNA < 50 (200) copies/mL at each study week with exact 95% confidence intervals.

Figure: Plot of the proportions of participants with HIV-1 RNA < 50 (200) copies/mL at each study week with exact 95% confidence intervals.

11.5 CD4+ cell count

Table: Mean (95% confidence interval), standard deviation, min, max, median, 25^{th} and 75^{th} percentile of CD4+ T-cell counts at all scheduled study weeks.

Table: Mean (95% confidence interval), standard deviation, min, max, median, 25^{th} and 75^{th} percentile of CD4+ T-cell count changes from baseline at all scheduled study weeks.

Figure: Plot of the mean CD4 T-cell count at each study week with 95% confidence intervals.

Figure: Plot of the mean CD4 T-cell count change at each study week with 95% confidence intervals.

11.6 HIV-1 drug resistance mutations in participants with virologic failure

List: HIV-1 drug resistance mutations by participants

11.7 Lipid and creatinine values [Not done for interim analysis]

Table: Mean (95% confidence interval), standard deviation, min, max, median, 25^{th} and 75^{th} percentile of creatinine, total cholesterol (fasting), triglycerides, LDL cholesterol (fasting), HDL cholesterol (fasting), and glucose (fasting) at all scheduled study weeks.

Table: Mean (95% confidence interval), standard deviation, min, max, median, 25^{th} and 75^{th} percentile of creatinine, total cholesterol (fasting), triglycerides, LDL cholesterol (fasting), HDL cholesterol (fasting), and glucose (fasting) changes from baseline at all scheduled study weeks.

Figure: Plot of the mean creatinine, total cholesterol (fasting), triglycerides, LDL cholesterol (fasting), HDL cholesterol (fasting), and glucose (fasting) at each study week with 95% confidence intervals.

11.8 Sign/symptoms (including Grade 2 rash) or laboratory toxicities of Grade 3 or higher, or of any grade which led to a permanent change in or discontinuation of study treatment

Table: Summary of Grade 2 rash and other adverse events Grade 3 or higher, or of any grade which led to a permanent change in or discontinuation of study treatment with onset date on or after the initiation of study treatment [EVW0314] by type (sign/symptom, diagnosis, laboratory measurement, and death) giving the number (%) of participants within each category and overall.

List: Listing of all signs/symptoms (including Grade 2 rash) or laboratory toxicities of grade 3 or higher or which led to permanent change in or discontinuation of study treatment [EVW0314], including participant (publicid), scheduled study week of the event, the type of event (sign/symptom, laboratory measurement), the specific name of the event, whether the event was resolved, the event grade, and whether the event was related to study treatment. Associated events will be indented to the associated primary events.

12 Exploratory Outcome Measure [Not done for interim analysis]

12.1 HIV-1 minority variants in participants with virologic failure

List: HIV-1 minority variants by participants.