

*This is ACTG A5327 Cohort 2 SAP Version 2.0 with names of authors, names of publication writing team members and analysis timeline redacted.*

**ACTG A5327**

**Cohort 2**

**STATISTICAL ANALYSIS PLAN**

**Sofosbuvir-Containing Regimens Without Interferon For Treatment of  
Acute HCV in HIV-1 Infected Individuals (SWIFT-C)**

**ClinicalTrials.gov Identifier: NCT02128217**

**Version 2.0:**

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## 1 Introduction

This document describes the content proposed for the primary statistical analysis of ACTG A5327. The focus of this analysis will address the primary safety and efficacy objectives for Cohort 2 (8 weeks of treatment) as well as the secondary objectives for which data will be available at the time of the primary analysis. Details about analyses for review by the Study Monitoring Committee (SMC) are not included in this SAP as all participants had completed study treatment by the time of preparation of this SAP and no further reviews of the study by the SMC were to be undertaken.

## 2 Study Overview

### 2.1 Study Schema

#### (Extracted from Protocol Version 2.0)

#### DESIGN

SWIFT-C is a Phase I, open-label, two-cohort clinical trial, in which between 44 and 50 acutely HCV-infected HIV-1 positive participants will be enrolled and administered oral sofosbuvir (SOF) in combination with weight-based ribavirin (RBV, cohort 1) or ledipasvir (LDV, cohort 2).

The study will investigate the safety and efficacy of two SOF-containing regimens and will assess if the addition of a second DAA allows for a shortened course of therapy. The study will open the first cohort with sofosbuvir plus ribavirin (SOF+RBV) for 12 weeks and with a planned accrual of at least 17 participants. The second cohort will open with ledipasvir/sofosbuvir (LDV/SOF) for an 8-week treatment. The second cohort will include at least 27 participants. Each cohort will occur in two steps: on treatment (Step 1) and followup (Step 2). The cohorts will enroll sequentially.

#### DURATION

32-36 weeks (8-12 weeks on-treatment followed by 24 weeks of follow-up)

#### SAMPLE SIZE

A minimum of 44 participants will be enrolled in Cohort 1 and Cohort 2.

Cohort 1: Minimum of 17 participants will be enrolled.

Cohort 2: Minimum of 27 participants will be enrolled.

If a participant is discontinued from study treatment for non-virologic reasons or is not evaluable for SVR12 while enrollment is ongoing to the same cohort, then an additional participant may be enrolled to that cohort to help ensure that an adequate number complete study treatment and are evaluable for SVR12, up to a maximum enrollment of 50 participants.

#### POPULATION

HIV-1 coinfecting individuals who have acute HCV infection or reinfection and have any genotype (Cohort 1) and genotype 1 or 4 (Cohort 2).

#### REGIMEN

Cohort 1: SOF 400mg once daily and weight-based RBV (1000 or 1200 mg daily in two divided doses).

Cohort 2: Daily fixed combination pill of LDV/SOF (90mg/400mg).

## 2.2 Hypothesis

An interferon sparing regimen of sofosbuvir (SOF) and ribavirin (RBV) and/or ledipasvir/sofosbuvir (LDV/SOF) can achieve sustained virologic response (SVR) 12 rates that are noninferior to the current standard of care assessed by historical control for the treatment of acute HCV in HIV-1/HCV co-infected individuals with an improved safety profile and a shorter length of treatment.

## 2.3 Primary Objectives

1. To evaluate HCV treatment response to SOF and weight-based RBV (1000 or 1200 mg daily in two divided doses) taken for 12 weeks and daily LDV/SOF taken for 8 weeks as assessed by SVR12, defined as HCV RNA undetectable [ $<$ lower limit of quantification (LLOQ) target not detected (TND)] 12 weeks post-treatment in persons with existing HIV-1 infection who are acutely infected with any HCV genotype (Cohort 1) or Genotype 1 or 4 (Cohort 2).
2. To evaluate the safety and tolerability of combination oral antiviral therapy with SOF and weight-based RBV taken for 12 weeks and daily LDV/SOF taken for 8 weeks in persons with existing HIV-1 infection who are acutely infected with any HCV genotype (Cohort 1) or Genotype 1 or 4 (Cohort 2).

## 2.4 Secondary Objectives

1. To evaluate the antiviral efficacy of SOF and weight-based RBV and LDV/SOF as measured by the proportion of participants with HCV RNA undetectable ( $<$ LLOQ TND) at weeks 1, 2, 4, 8, 12 and at 2 (SVR2), 4 (SVR4), 8 (SVR8), 12 (SVR12) and 24 (SVR24) weeks post-treatment.
2. To evaluate evidence of relapse, defined as HCV RNA undetectable ( $<$ LLOQ TND) at end-of-treatment but HCV RNA quantifiable ( $\geq$ LLOQ) during followup.
3. To assess the emergence of viral resistance to SOF and LDV when administered with RBV for acute HCV infection.
4. To estimate RBV pharmacokinetics (PK) and evaluate covariates (including concomitant antiretroviral drugs) which may affect RBV PK. (Cohort 1 only)
5. To assess the relationship of viral clearance and RBV PK (Cohort 1) with baseline predictors including genetic polymorphisms (eg., IL28B and ITPA), expression of key host immune response genes and proteins.

6. To assess the effects of LDV on PK or tenofovir (TFV) in persons on tenofovir disoproxil fumarate (TDF)-containing regimens. (Cohort 2 only)
7. To evaluate participants' adherence by using several tools, including self-report, pill count, and drug concentrations.
8. To evaluate the hypothesis that successful direct-acting antiviral (DAA)-based therapy alleviates type I (IFN)-induced immune dysfunction during acute HCV infection.

## 2.5 Visit and Evaluation Schedule

The Cohort 2 expected schedule for on-treatment clinic visits is shown in Table 1 and the expected schedule for post-treatment follow up clinic visits is shown in Table 2 below. Unless otherwise noted, analyses by A5327 study week will utilize these study week definitions (defined in days); the start time for calculation of study week will be the date of first dose of treatment.

**Table 1: Weeks Since Starting Treatment**

	Baseline	Week 1	Week 2	Week 4	Week 8
Days	0	4-10	11-17	21-42	49-70

**Table 2: Weeks Since Starting Post-Treatment Follow up**

	Week 0	Week 2	Week 4	Week 8	Week 12	Week 24
Days	Last day of treatment	9-22	23-49	51-78	79-112	161 onwards

## 2.6 A5327 Protocol History

**The analysis described in this SAP concerns only Cohort as defined in protocol version 2.0:**

### **Cohort 2:**

Protocol Version 2.0 (finalized on July 2, 2015)

A5327 Clarification Memo 1, Version 2.0 (10/08/15) regarding negative pregnancy tests.

## 2.7 General Statistical Considerations

Key analysis decisions:

- Throughout, study entry is defined at the date of entry visit as recorded as the header date on the ADM0010.

- The analyzed measurement will, in general, be the measurement closest to the scheduled evaluation time, and the acceptable windows will be based on time since first study treatment dose.
- Data summaries and analyses will be presented for Cohort 2 only (the analysis of data for participants in Cohort 1 are included in a separate report).

Notes for conventions used in the primary analysis report:

- For the primary analysis report:
  - Lists will be sorted by variables in the order given with study participants identified using an alternate patient identifier (PubID, i.e. not ACTG patid).
  - Participant-specific dates will not be shown, but converted to time since start of study treatment (all participants did start study treatment).
- Each Table/Figure/Listing will be annotated with the name and location of the program used to create it.
- Validation:
  - Tables/figures requiring SDAC validation of the program used to generate the results will be flagged with “[V]”.
  - Tables/figures requiring independent programming of results by the SDAC validator will be flagged with “[IP]”.

### **3 Accrual and Screening [V]**

Purpose : To give a summary of accrual and the distribution of enrollment across sites.

- a) Table: Number (%) enrolled overall and by month

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

- b) Table: Number (%) enrolled by enrolling site  
c) List: participants who were screened by did not enter the study (screen failures)

### **4 Eligibility Violations and Exclusions [V]**

Purpose: To document why any participants who were enrolled were subsequently excluded from analysis and document any other exclusions.

- a) List: violations of eligibility criteria by site and details of exclusions from analyses (if any)  
b) List: participants who did not have treatment dispensed. These participants will be excluded from the analysis.

### **5 Baseline Characteristics [V]**

Purpose: To describe the study population

Baseline characteristics will be analyzed as continuous or as categories or both, as appropriate. Tables will provide # of participants, # of missing data points, median, quartiles (Q1-Q3), minimum, maximum for the continuous variables (with transformations as appropriate) and number (%) for the categorical variables. In calculation of percentages, participants with missing data will not be included in the denominator.

a) Table summarizing demographic characteristics

- i. Sex (STATUS): number (%)
- ii. Self-reported race/ethnicity (STATUS): number (%)
- iii. Age on the day of study entry (years) (STATUS): N, median, 1st and 3rd quartile, minimum and maximum; number (%) by age group (18-19, 20-29, 30-39, 40-49, 50-59; 60-69; 70+ years, rounded down)
- iv. Intravenous drug use (IVD) history (STATUS): number (%) by group (Never, current, previous user)
- v. Weight (kg) (F0033): N, median, 1st and 3rd quartile, minimum and maximum
- vi. BMI (kg/m<sup>2</sup>): number (%) by BMI group (Underweight[<18.5], normal [18.5-24.9], overweight [25-29.9], obese [>30])

b) Table summarizing HCV disease status

- i. Infection status (ANSTAB): number (%) by new acute HCV infection and HCV reinfection
- ii. Acute HCV eligibility (ANSTAB): number (%) meeting one of the acute HCV infection criteria from protocol section 4.1.2
- iii. Time from first laboratory evidence of acute HCV to entry (days) (ANSTAB): N, median, 1st and 3rd quartile, minimum and maximum
- iv. Time from diagnosis of acute HCV to entry (days) (DF0002): N, median, 1st and 3rd quartile, minimum and maximum
- v. Baseline HCV RNA (IU/ml) and corresponding results for log<sub>10</sub> copies/ml (F3116): N, median, 1st and 3rd quartile, minimum and maximum  
Note: Baseline is defined as the value at A5327 entry
- vi. Baseline HCV RNA: number (%) undetectable and detectable, number (%) < 6 million IU/mL and ≥6 million IU/mL  
Note: undetectable at baseline may indicate spontaneous clearing occurring between screening and baseline.
- vii. HCV genotype (SRW0028): number (%) by category (1a, 1b, 2a, 2b, 3, 4, 5, 6)
- viii. IL28B genotype (GENOHUM): number (%) by category (CC, CT, TT)  
Note: Batch tested at the end of study.

c) Table summarizing HIV disease status

- i. Baseline HIV-1 RNA (copies/ml) (RNALDMS): number (%) by category (<50 copies, ≥50 copies)  
Note: Baseline is defined as the closest value on/before date of start of study treatment.



- ii. Baseline CD4+ cell count (/mm<sup>3</sup>) (LBW0054): N, median, 1st and 3rd quartile, minimum and maximum;  
Note: Baseline is defined as the arithmetic mean of screening and entry values or, in the absence of one value, the one available.
  - iii. Baseline CD4+ cell percent (LBW0054): N, median, 1st and 3rd quartile, minimum and maximum;  
Note: Baseline is defined as the arithmetic mean of screening and entry values or, in the absence of one value, the one available.
- d) Table summarizing HIV-1 antiretroviral therapy (ARVs)
- i. Receiving HIV ARVs prior to entry (ANSTAB): number (%) yes and no
  - ii. HIV ARV regimen at entry (TXT0004): number (%) on each regimen
  - iii. HIV ARV regimen of interest for renal functions (TXT0004): number (%) on TDF + boosted PI, COBI, and other ARV regimens
  - iv. NNRTIs (TXT0004): number (%) on efavirenz, rilpivirine, tenfovir, and abacavir based regimens
  - v. Integrase Inhibitors (IIs) (TXT0004): number (%) on raltegravir and dolutegravir based regimens
  - vi. Protease Inhibitors (PIs) (TXT0004): number (%) on boosted PI based regimens
- e) Table summarizing baseline laboratory evaluations
- For each laboratory evaluation the following will be presented unless otherwise specified: N, median, 1st and 3rd quartile, minimum and maximum. If the lab value is graded, DAIDS grading scale will also be presented.
- Note: Baseline is defined as the last available value on or before the date of starting study treatment. Fasting per protocol is defined as nothing to eat or drink except prescription medications and water for at least 8 hours prior to the procedure. If nonfasting at the screening visit, the participant should return within 7 days for fasting blood draw. These panels are performed at the designated testing laboratory; see A5237 lab processing chart [LPC] for directions.
- i. Hematology characteristics (F2850): hematocrit, hemoglobin (g/dL), platelets (cells/mm<sup>3</sup>), red blood cell (RBC) count, white blood cell (RBC) count (cells/mm<sup>3</sup>), WBC differentials (absolute and percentage: lymphocytes, monocytes, neutrophils, eosinophils, basophils, reticulocyte count) and mean corpuscular volume (MCV).
  - ii. Chemistry characteristics(F2841): alanine aminotransferase (ALT/SGPT), aspartate aminotransferase (AST/SGOT), albumin (g/dL), alkaline phosphatase, creatinine, total bilirubin, direct bilirubin, glucose (mg/dL), lipase, potassium (mEq/L), thyroid-stimulating hormone, sodium(mEq/L) and gamma-glutamyl transferase.
  - iii. Calculated creatinine clearance(LBW0060)
  - iv. Fasting Lipids (LDMS table TBD): low density lipoprotein (LDL, mg/dL), high density lipoprotein (HDL, mg/dL), triglycerides (TG, mg/dL), total cholesterol (TC, mg/dL), and apolipoproteins B, E, and CII.

- v. Coagulation Markers (F2850): INR, prothrombin time (PT), activated partial thromboplastin (APTT)
  - vi. Urinalysis (F0869): appearance, blood, color, glucose, leukocyte esterase, PH, protein, urobilinogen
- f) Table summarizing history of sexually transmitted infections (STIs)
- i. Reported History of STI Diagnosis (DF0002): number (%) with history of STIs and no history of STIs. Within history of STIs, number (%) for each type of STI. Refer to A5327 Targeted Diagnosis list on the protocol specific web page, under Genitourinary/Sexually Transmitted Diseases, with the addition of acute Hepatitis B, herpes simplex virus and cervicitis.

## 6 Study status and loss to follow up [V]

Purpose: To summarize extent of follow-up on study.

- a) CONSORT diagram: number of participants enrolled, number who started treatment, completed treatment, and completed study
- b) Table: On study treatment number (%) by category (F4003 and F1601)  
Categories included are:
  - i. Completed planned treatment period and post treatment follow-up
  - ii. Completed planned treatment period but off study early
  - iii. Discontinued study treatment early and completed planned post treatment follow-up
  - iv. Discontinued study treatment early and discontinued post treatment follow-up early
- c) List: Reasons off study treatment early (include both the category and text field from F4003)
- d) List: Reasons off study early (include both the category and text field from F1601)

## 7 Study conduct [V]

Purpose: To summarize how compliant participants are with study visits  
Table: summarize missed visits reflected as the number (%) of expected and observed clinic visits

## 8 Primary Endpoint Analyses

### 8.1 Efficacy Outcome [IP]

Note: For clarity of presentation, results for the primary efficacy outcome and for the secondary efficacy outcomes concerning HCV RNA will be presented together in the analysis report.

Primary Outcome Measure (from protocol section 9.2.1.1)

SVR12 is defined as HCV RNA undetectable (<LLOQ TND) of the assay at 12 weeks after date of last dose of study treatment.

The 12 week measurement will be the measurement obtained closest to 84 days (i.e. 12\*7 days), within the window 79 to 112 days inclusive after study treatment discontinuation. This analysis will be intent to treat (ITT) analysis.

If a participant has no HCV RNA measurement within this window, then the participant will be considered as having detectable HCV RNA at 12 weeks unless the preceding and subsequent HCV RNA measurements are both undetectable (<LLOQ TND).

### Planned Analysis

- a) Table: summarize proportion and two-sided 90% confidence interval around the observed SVR12 proportion using the Blyth-Still-Casella(BSC) method for binomial outcomes (HCVRNALDMS)
- b) Table: summarize proportion and two-sided 90% confidence interval around the observed SVR12 proportion of participants who are evaluable for SVR12 but exclude participants who prematurely discontinue study treatment for nonvirologic reasons (Completer Analysis) using the Blyth-Still-Casella(BSC) method for binomial outcomes (HCVRNALDMS)

## **8.2 Safety Outcome [IP]**

Note: For clarity of presentation, results for the primary safety outcome and for the secondary safety outcomes will be presented together in the analysis report.

### Primary Outcome Measure (from protocol section 9.2.1.2)

Occurrence of a Grade  $\geq 2$  AE (diagnosis, sign, symptom, or laboratory abnormality), SAE according to ICH criteria, or treatment-limiting AE (i.e., an AE reported as the reason for permanent discontinuation of study treatment).

Any event occurring after initiation of study treatment through to 28 days after date of last dose of study treatment will be included (except that an event that is ongoing at the same grade from before start of study treatment will be excluded).

### Planned Analysis

- a) Table: summarize proportion and two-sided 90% confidence interval around the proportion of participants who have one of the defined AEs (EVW0206, EVW0207)
- b) Table: list of all events meeting the primary safety outcome definition (including weeks from start of study treatment, type of AE, grade, whether or not an SAE, whether or not it was a treatment limiting AE)

## 9 Secondary Outcome Measures Analyses

### 9.1 HCV RNA while on study treatment [V]

Note: A figure showing each participant's  $\log_{10}$  HCV RNA trajectory including on-treatment and post-treatment periods will be included. An appendix to the report will be included listing scheduled measurement weeks, calculated weeks of each measurement, HCV RNA value,  $\log_{10}$  HCV RNA value, and reason for any missed measurement.

Secondary Outcome Measure (from protocol section 9.2.2.1)

HCV RNA undetectable (<LLOQ TND) at 1, 2, 4, and 8 weeks after starting study treatment. Measurements will be assigned to these times within windows of 4 to 10, 11 to 17, 21 to 42, and 49 to 70 days, inclusive, respectively. If there is more than one measurement within a window, then the measurement closest to the targeted time will be used. If there is no measurement within a window, then the participant will be considered as having detectable HCV RNA at the targeted time, unless both the preceding and succeeding measurements are undetectable (<LLOQ TND).

Planned Analysis

- a) Table: summarize the proportion of HCV undetectable (<LLOQ TND) of the assay at 1, 2, 4, 8 weeks after starting study treatment. A 90% two-sided confidence interval will be provided around the observed proportions (HCVRNALDMS)

### 9.2 HCV RNA during follow-up [V]

Secondary Outcome Measure (from protocol section 9.2.2.2)

HCV RNA undetectable (<LLOQ TND) at 2 (SVR2), 4 (SVR4), 8 (SVR8), and 24 (SVR24) weeks after last dose of study treatment. The windows for these measurements will be 9 to 22, 23 to 50, 51 to 78, and 161 days onwards. If there is more than one measurement within a window, then the measurement closest to the targeted time will be used. If there is no measurement within a window, then the participant will be considered as having detectable HCV RNA at the targeted time, unless (for weeks 4 and 8) the preceding and subsequent HCV RNA measurements are both <LLOQ TND.

Planned Analysis

Note: For clarity of presentation, results for the primary outcome measure (SVR12) will be included in the following tables.

- a) Table: summarize the proportion of HCV undetectable (<LLOQ TND) of the assay at 2 (SVR2), 4 (SVR4), 8 (SVR8), 12 (SVR12) and 24 (SVR24) weeks after last dose of study treatment. A 90% two-sided confidence interval will be provided around the observed proportions (HCVRNALDMS)
- b) Figure: summarize the proportion of HCV undetectable, with the upper and lower limit of the confidence interval at 2 (SVR2), 4 (SVR4), 8 (SVR8), 12 (SVR12) and 24 (SVR24) weeks after last dose of study treatment (HCVRNALDMS).

### 9.3 HCV RNA Relapse [V]

#### Secondary Outcome Measure (from protocol section 9.2.2.3)

To evaluate virologic evidence of relapse, defined as HCV RNA undetectable (<LLOQ TND) at end-of-treatment but HCV RNA quantifiable ( $\geq$ LLOQ) during followup, will require confirmation and should be performed as soon as possible but within 2 weeks after determination of initial observation.

For analysis purposes, confirmatory values obtained after 2 weeks will be included.

#### Planned Analysis

- a) List: Participants who have virologic evidence of relapse. The listing will include week of HCV RNA undetectable (<LLOQ TND), HCV RNA undetectable at end of study treatment, post treatment week of HCV RNA detectable ( $\geq$ LLOQ) and confirmation of HCV RNA detectability (HCVRNALDMS)

### 9.4 SOF or LDV-associated resistance mutations

#### Secondary Outcome Measure (from protocol section 9.2.2.4)

Development of SOF or LDV-associated resistance mutations. The set of mutations to be considered will be defined at the time of analysis based on information from other studies available at that time.

#### Planned Analysis

- a) The analysis will be performed outside of SDAC. The raw data will be downloaded to the final database using the GETBSS HCV script.

### 9.5 AEs by type of event [V]

#### Secondary Outcome Measure (from protocol section 9.2.2.5)

Occurrence of the AEs detailed in section 9.2.1.2 of the protocol (Section 9.1 in this document) by type of event. Type of events include: diagnosis, sign, symptom, laboratory abnormality, SAE according to ICH criteria, or treatment-limiting AE. Additional analysis of selected renal safety parameters is included because of a concern that participants taking TDF might be at increased risk for such events.

#### Planned Analysis

- a) Table: list of events (EVW0206, EVW0207), including HIV ARV regimen.
- b) Table: summarizing creatinine clearance and urinalysis during on study treatment by participants who were taking TDF in combination either with a boosted PI or with COBI and participants taking other HIV ARV regimens.
- c) Figure: Individual participant plots of creatinine clearance over time distinguishing participants who took TDF with a boosted PI, from participants who took TDF with COBI, from other participants.

- d) Table of protein urinalysis results at each scheduled measurement week distinguishing participants taking TDF with either a boosted PI or COBI from other participants: Number (%) in each protein category.

## **9.6 Change in HIV-1 RNA [V]**

### Secondary Outcome Measure (from protocol section 9.2.2.6)

Change in HIV-1 RNA from last measurement prior to start of study treatment to each subsequent scheduled HIV-1 RNA measurement time: for participants on ART at study entry, these will be categorized as changes from <50 copies/mL to ≥50 copies/mL, or vice versa; for participants not on ART at study entry, quantitative change in log<sub>10</sub> HIV-1 RNA will be considered. Windows for measurements to be included and the algorithm for selecting measurements within each window will be as described for HCV RNA measurements above.

### Planned Analysis

Each analysis will be done by ARV use at study entry (yes vs no) (RNALDMS, HXW0171)

- a) Table: summarize HIV-1 RNA measurements at each time point
- b) Table: summarize HIV-1 RNA changes from last measurement prior to study treatment to each subsequent HIV-1 RNA measurement
- c) Figure: summarize HIV-1 RNA measurements at each time point
  - i. For participants on ARVs at study entry: the figure will summarize the proportion of participants who had HIV-1 RNA < 50 copies/mL with 95% confidence interval around the proportion
  - ii. For participants not on ARVs at study entry: the figure will summarize the HIV-1 RNA median and IQR (Q1, Q3)
- d) Figure: summarize HIV-1 RNA changes at each time point
  - i. For participants on ARVs at study entry: the figure will summarize the proportion of participants who had HIV-1 RNA < 50 copies/mL with 95% confidence interval around the proportion
  - ii. For participants not on ARVs at study entry: the figure will summarize the HIV-1 RNA median and IQR (Q1, Q3)

## **9.7 Change in CD4+ cell count and CD4+ cell percentage [V]**

### Secondary Outcome Measure (from protocol section 9.2.2.7)

Change in CD4+ cell count from last measurement prior to start of study treatment to each subsequent scheduled CD4+ cell count measurement time. Windows for measurements to be included and the algorithm for selecting measurements within each window will be as described for HCV RNA measurements above.

### Planned Analysis

- a) Table: summarize CD4+ cell count and percentage measurements at each time point (LBW0054: N, median, 1st and 3rd quartile, minimum and maximum)

- b) Table: summarize CD4+ cell count and percent changes from the last measurement prior to study treatment to each subsequent CD4+ cell count measurement (LBW0054: N, median, 1st and 3rd quartile, minimum and maximum)
- c) Figure: summarize CD4+ cell count and percentage median and IQR (Q1, Q3)
- d) Figure: summarize CD4+ cell count and percent change median and IQR (Q1, Q3)

## 9.8 Adherence [V]

### Secondary Outcome Measure (from protocol section 9.2.2.8)

Measures of adherence: for each LDV/SOF at each visit: (a) self-reported adherence as measured by whether or not a participant reports having taken all doses; and (b) proportion of doses taken since the previous visit as determined by pill count.

### Planned Analysis

- a) Table: summarize proportion of participants taking all doses of medication within the 3 days prior to the evaluation (QL0757)
- b) Table: summarize the number (%) of doses taken since the previous visit, along with descriptive statistics (N, median, 1st and 3rd quartile, minimum and maximum) (EVW0320)

## 9.9 Immune Parameters

### Secondary Outcome Measure (from protocol section 9.2.2.9)

Immune parameters: changes in magnitude of induction of ISGs by Nanostring, changes in IP-10 levels, and changes in T cell function (CD4+ proliferative and CD8 CTL assays) at end of treatment and end of followup compared to study entry. Analysis will be performed as a function of IL28B genotype.

### Planned Analysis

The analysis plan may be updated with additional analysis for this secondary outcome. Immune parameter tables are TBD.

- a) Table: summarize ISGs at each time point and change in ISG from baseline
- b) Table: summarize IP-10 levels at each time point and change in IP-10 from baseline
- c) Table: summarize T cell function at each time point and change in T cell function from baseline

## 9.10 Pharmacology Analysis

A separate Statistical Analysis Plan will be developed for the Pharmacology objectives.

## 10 Analysis datasets

Preliminary list of analysis datasets [V]

**baseline [V]** – key baseline variables used in multiple summaries

**studystatus [V]** – study status information, e.g. on study, off study, reason off study

**screeninfo [V]** – screening failures

**hivrna [V]** – longitudinal HIV-1 RNA with calculated study weeks

**cd4 [V]** – longitudinal CD4 cell count with calculated study weeks

**arv2 [V]** – HIV-1 antiretrovirals at entry and during study

**hcvrxadhere [V]** – adherence to study drugs with calculated study weeks

**primsafe[IP]** – primary safety events with calculated weeks on treatment

**hcvrna[IP]** – primary efficacy analysis with longitudinal HCV RNA with calculated study weeks

NOTE: Other datasets that are created will be added in a later version of this document.