STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 2, Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Sofosbuvir/Velpatasvir Fixed Dose Combination in Subjects with Chronic HCV Infection Who Have Received a Liver Transplant
Name of Test Drug:	Sofosbuvir/Velpatasvir Fixed-Dose Combination
Study Number:	GS-US-342-2104
Protocol Version/Date:	Original/19 February 2016
Analysis Type:	Final Analysis (SVR12)
Analysis Plan Version:	Version 1
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Analysis Plan Author:	PPD

CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

AE	adverse event
ALT	alanine aminotransferase
APTT	activated partial thromboplastin time
AST	aspartate transaminase
ATC	anatomical therapeutic chemical
BLQ	below the limit of quantitation
BMI	body mass index
BPM	beats per minute
CI	confidence interval
CSR	clinical study report
DAA	direct acting antiviral
ECG	Electrocardiogram
eCRF	electronic case report form
eCrCl	estimated creatinine clearance
EOT	end of treatment
FAS	full analysis set
FDC	fixed dose combination
FU	follow-up
GGT	gamma-glutamyl transferase
HbsAg	hepatitis B surface antigen
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HLGT	high level group term
HLT	high level term
ID	Identification
INR	international normalized ratio for prothrombin time
IWRS	Interactive Web Response System
LLT	lower level term
LLOQ	lower limit of quantitation
MCV	mean corpuscular volume
MDMA	Methylenedroxymethamphetamine
MedDRA	Medical Dictionary for Regulatory Activities
PD	Pharmacodynamics
PEG	pegylated interferon
PK	Pharmacokinetics
PT	preferred term
Q1	first quartile
Q3	third quartile

RBC	red blood cells
RBV	Ribavirin
RNA	ribonucleic acid
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SOC	system organ class
SOF	sofosbuvir (Sovaldi®)
SVR	sustained virologic response
SVRx	sustained virologic response x weeks after stopping study drug
TE	treatment-emergent
TFLs	tables, figures, and listings
TND	target not detected
ULN	upper limit of the normal range
VEL	velpatasvir (previously GS-5816)
WBC	white blood cell
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures, and listings (TFLs) in the clinical study report (CSR) for Study GS-US-342-2104. This SAP is based on the original protocol dated 19 February 2016 and the electronic case report form (eCRF). The SAP will be finalized before data finalization. Any changes made after the finalization of the SAP will be documented in the CSR.

1.1. Study Objectives

The primary objectives of this study are as follows:

- To evaluate the efficacy of study treatment with sofosbuvir (SOF)/velpatasvir (VEL, GS-5816) fixed dose combination (FDC) for 12 weeks as measured by the proportion of subjects with sustained virologic response 12 weeks after cessation of study treatment regimen (SVR12)
- To evaluate the safety and tolerability of the study treatment regimen

The secondary objectives of this study are as follows:

- To determine the proportion of subjects who attain SVR at 4 weeks after cessation of treatment regimen (SVR4)
- To evaluate the kinetics of circulating HCV RNA during study treatment and after cessation of study treatment regimen
- To evaluate the emergence of viral resistance to SOF and VEL during study treatment and after cessation of study treatment regimen

The exploratory objectives of this study are as follows:

PPD

1.2. Study Design

This is a multicenter, open-label, Phase 2 study that will evaluate the safety and efficacy of SOF/VEL FDC for 12 weeks in subjects with chronic HCV who have received a liver transplant.

Approximately 80 subjects with recurrent HCV post-liver transplant will be enrolled and treated with SOF/VEL FDC tablet once daily for 12 weeks. The enrollment target for subjects with HCV

genotype 3 infection is approximately 20%; and the enrollment target for subjects with Metavir stage 3 or 4 fibrosis/cirrhosis or corresponding fibrosis degree is approximately 20%.

The schedule of assessments is provided in Appendix 2 of the study protocol.

The total time to complete all study visits is approximately 28 weeks (30 weeks for those requiring liver biopsy or additional HCV genotyping at screening), as described below:

- 28-day screening period (can be extended up to 42 days if liver biopsy or additional HCV genotyping is required or for extenuating circumstances)
- A 12-week study treatment period
- Up to 12-week post study treatment period

1.3. Sample Size and Power

Due to the exploratory nature of this study, no formal power calculations were used to determine sample size. The sample size was selected based on practical reasons.

With a sample size of 80, the 95% confidence interval will extend at most 23% in length.

2. TYPE OF PLANNED ANALYSIS

2.1. Data Monitoring Committee

This study does not have a Data Monitoring Committee.

2.2. Final Analysis

After all subjects have completed the study, outstanding data queries have been resolved, and the database has been cleaned and finalized, the final analysis of the data will be performed.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

Analysis results will be presented using descriptive statistics. For categorical variables, the number and percentage of subjects in each category will be presented; for continuous variables, the number of subjects [n], mean, standard deviation [SD], median, first quartile [Q1], third quartile [Q3], minimum, and maximum will be presented.

Data collected in the study will be presented in by-subject listings for all subjects in the Safety Analysis Set, unless otherwise specified. All by-subject listings will be presented by subject identification (ID) number in ascending order, unless otherwise specified.

3.1. Analysis Sets

Analysis sets define the subjects to be included in an analysis. Analysis sets and their definitions are provided in this section. The number of subjects eligible for each analysis set will be provided. Subjects who were excluded from each analysis set will be summarized or provided in a by-subject listing with reasons for exclusion.

3.1.1. All Enrolled Analysis Set

The All Enrolled Analysis Set includes all subjects who were enrolled into the study. Subjects will be grouped by assigned treatment at enrollment (ie, SOF/VEL 12 Weeks).

3.1.2. Full Analysis Set

The Full Analysis Set (FAS) includes all enrolled subjects who took at least 1 dose of the study drug. Since all subjects in this study were assigned to and received SOF/VEL for 12 Weeks, the FAS will be the same as the Safety Analysis Set.

This is the primary analysis set for efficacy analyses.

3.1.3. Safety Analysis Set

The Safety Analysis Set includes all subjects who took at least 1 dose of the study drug. Subjects are grouped within the Safety Analysis Set according to the treatment they actually received.

This is the primary analysis set for safety analyses.

3.1.4. Pharmacokinetic Analysis Set

The Pharmacokinetic (PK) Analysis Set includes all subjects who took at least 1 dose of the study drug and have at least 1 nonmissing postdose concentration value for the corresponding analyte in plasma. The analytes of interest may include SOF and its metabolites GS-566500 and GS-331007, and VEL. The PK analysis set will be used for analyses of population PK. Subjects will be grouped according to the treatment they actually received.

3.2. Subject Grouping

The treatment group for all subjects will be “SOF/VEL 12 Weeks”.

In general, the efficacy analyses will be performed for the FAS overall and by HCV genotype (1 total [and further broken down for 1a and 1b], 2, 3, 4, 5, and 6). The primary analysis will be performed for the “SOF/VEL 12 Weeks” group as described in Section 6.1. HCV genotype will be determined by Covance laboratories using the LiPA 2.0 assay or by Sanger NS5B population sequencing when results from LiPA 2.0 are unsuccessful, "indeterminate", or resulted in "mixed genotype" and to determine genotype 1 subtype if it is not reported.

The safety analyses will be performed for “SOF/VEL 12 Weeks” using the Safety Analysis Set.

3.3. Strata and Covariates

There are no strata or covariates for this study.

3.4. Examination of Subject Subsets

Subject subsets will be explored overall and by HCV genotype (1 total [and further broken down by 1a, 1b], 2, 3, 4, 5, and 6) for the primary efficacy endpoint, SVR12, including the following:

- age (< 65 years, ≥ 65 years)
- sex at birth (male, female)
- race (white, black, all other races)
- ethnicity (Hispanic or Latino, non-Hispanic or Latino)
- baseline BMI (< 30 kg/m2, ≥ 30 kg/m2)
- cirrhosis (no, yes)
- baseline HCV RNA (< 800,000 IU/mL, ≥ 800,000 IU/mL)
- baseline alanine aminotransferase (ALT) (≤ 1.5 × upper limit of normal [ULN], > 1.5 × ULN)

- IL28B (CC, non-CC; with non-CC further broken down to CT, TT)
- prior HCV treatment (treatment naive, treatment-experienced)
- prior HCV treatment experience and cirrhosis status (ie, treatment naive with cirrhosis, treatment-experienced with cirrhosis, treatment naive without cirrhosis, treatment-experienced without cirrhosis)

3.5. Multiple Comparisons

No multiplicity adjustment will be made since SVR12 is the primary efficacy endpoint.

3.6. Missing Data and Outliers

3.6.1. Missing Data

In general, missing data will not be imputed unless methods for handling missing data are specified.

For subjects with a missing last dose date of study drug, imputation rules are described in Section 3.8.1. The handling of missing or incomplete dates for adverse event (AE) onset is described in Section 7.1.5.2, and for prior and concomitant medications in Section 7.4.

For analyses of categorical HCV RNA data, missing posttreatment HCV RNA data will have the missing data imputed. Missing on-treatment HCV RNA will have missing data imputed up to the time of the last dose (for on-treatment displays). If the study day associated with the last dosing date of any study drug is greater than or equal to the lower bound of a visit window, and the value at the visit is missing, then the value will be imputed. If the study day associated with the last dosing date is less than the lower bound of a visit window then the on-treatment value at that visit will remain missing.

If an HCV RNA data point is missing and is preceded and followed in time by values that are "< LLOQ target not detected (TND)," then the missing data point will be set to "< LLOQ TND." If a data point is missing and preceded and followed by values that are "< LLOQ detected," or preceded by "< LLOQ detected" and followed by "< LLOQ TND," or preceded by "< LLOQ TND" and followed by "< LLOQ detected," then the missing value will be set to "< LLOQ detected." In these situations the data point will be termed a bracketed success; otherwise, the data point will be termed a bracketed failure (ie, ≥ LLOQ detected). If a data point is missing and is not bracketed, the missing data point will also be termed a failure (ie, ≥ LLOQ detected).

For the analyses of continuous HCV RNA efficacy data, when and only when a missing HCV RNA value is imputed as < LLOQ TND or < LLOQ detected according to the imputation rules described above, will the corresponding continuous value be imputed to LLOQ − 1 IU/mL. No other imputation will be performed for continuous HCV RNA data.

3.6.2. Outliers

Outliers will be identified during the data management and data analysis process, but no sensitivity analyses will be conducted. All data will be included in the data analysis.

3.7. Data Handling Conventions and Transformations

By-subject listings will be presented for all subjects in the Safety Analysis Set sorted by subject ID number, visit date, and time (if applicable) unless otherwise specified. Data collected on log forms, such as AEs, will be presented in chronological order for each subject.

Age (in years) on the date of the first dose of study drug and sex at birth will be used for analyses and presentation in listings.

If a subject was not dosed with study drug at all, then the date the informed consent was signed will be used in place of the first dose date of study drug for calculations. For some countries, only birth year is collected on the eCRF. In those cases, "01 January" will be used for the unknown birth day and month for the purpose of age calculation, unless age is captured on the CRF.

Non-PK data that are continuous in nature but are less than the lower limit of quantitation (LLOQ) or above the upper limit of quantitation will be imputed as follows:

- A value that is one unit less than the limit of quantitation will be used for calculation of descriptive statistics if the datum is reported in the form of "< x" (where x is considered the limit of quantitation). For example, if the values are reported as < 50 and < 5.0, values of 49 and 4.9, respectively, will be used for calculation of summary statistics. An exception for this rule is any value reported < 1. For the values reported as < 1 or < 0.1, value of 0.9 or 0.09 will be used for calculation of summary statistics.

- A value that is one unit above the limit of quantitation will be used for calculation of descriptive statistics if the datum is reported in the form of "> x" (where x is considered the limit of quantitation). Values with decimal points will follow the same logic as above.

- The limit of quantitation will be used for calculation of descriptive statistics if the datum is reported in the form of "≤ x" or "≥ x" (where x is considered the limit of quantitation).

The COBAS® AmpliPrep/COBAS® TaqMan® HCV Quantitative Test, version 2.0 was used to determine HCV RNA results in this study. The LLOQ of the assay is 15 IU/mL.

When the calculated HCV RNA IU/mL is within the linear range of the assay, then the result will be report as the "<< numeric value>> IU/mL." This result will be referred to in this document as the numeric result or as "≥ LLOQ detected" for the categorical result.

When HCV RNA is not detected, the result is reported as "No HCV RNA detected" or "target not detected". This result will be referred to in this document as "< LLOQ target not detected" or "< LLOQ TND."

When the HCV RNA IU/mL is less than LLOQ of the assay, the result is reported as "< 15 IU/mL HCV RNA detected." This result will be referred to in this document as "< LLOQ detected."

The overall category of HCV RNA < LLOQ includes "< LLOQ TND" and "< LLOQ detected."

For numerical HCV RNA data, values below LLOQ will be set to the LLOQ – 1 IU/mL (ie, 14 HCV RNA IU/mL). HCV RNA values returned as "target not detected" will also be set to LLOQ – 1 IU/mL.

If methods based on the assumption that the data are normally distributed are not adequate, analyses may be performed on transformed data (eg, $\log_{10}$ scale) or nonparametric analysis methods may be used, as appropriate.

3.8. Visit Windows

3.8.1. Definition of Study Day

Study day is the day relative to the date of the first dose of study drug. Study Day 1 will be defined as the day of first dose of study drug administration.

Study day will be calculated from the date of first dose of study drug administration and derived as follows:

- For postdose study days: Assessment Date – First Dose Date + 1
- For days prior to the first dose: Assessment Date – First Dose Date

The last dose date for the study drug will be the end date on study drug administration eCRF for the record where the "subject permanently discontinued" flag is 'Yes'.

If there are subjects for whom the date of last study drug is unknown due to the reason that the subject was lost to follow-up and not able to be contacted, the date of last dose will be estimated using the maximum of nonmissing study drug start or stop dates, visit dates, and laboratory collection dates (posttreatment visits and unscheduled visits are not included).

3.8.2. Analysis Windows

Subject visits might not occur on protocol-specified days. Therefore, for the purpose of analysis, observations will be assigned to analysis windows.

In general, the baseline value will be the last nonmissing value on or prior to the first dose date of study drug.

HCV RNA, vital signs, and safety laboratory data collected up to the last dose date + 3 days are considered to be on-treatment data and HCV RNA, vital signs, and safety laboratory data collected after the last dose date + 3 days are considered posttreatment data. The analysis windows for on-treatment HCV RNA, vital signs and safety laboratory data are provided in Table 3-1.

Table 3-1. Analysis Windows for On-treatment HCV RNA, Vital Signs and Safety Laboratory Data

	(SOF/VEL 12 Weeks)		
Nominal Visit	**Nominal Day**	**Lower Limit**	**Upper Limit**
Baseline[a]	1	(none)	1
Week 2	14	2	21
Week 4	28	22	42
Week 8	56	43	70
Week 12[a]	84	71	≥ 85

a Coagulation and urinalysis tests will only be collected at baseline and Week 12.

HCV RNA, vital sign, and safety laboratory data collected after the last dose date + 3 days will be assigned to a posttreatment follow-up (FU) visit. Visit windows will be calculated from the last dose date (ie, FU Day = collection date minus the last dose date) as shown in Table 3-2.

Table 3-2. Analysis Windows for Posttreatment HCV RNA, Vital Signs and Hematology/Chemistry Safety Laboratory Data

	HCV RNA			Vital Signs and Safety Laboratory Data[b]		
Nominal FU[a] Visit	**Nominal FU Day**	**Lower Limit**	**Upper Limit**	**Nominal FU Day**	**Lower Limit**	**Upper Limit**
FU-4	28	21	69	28	4	30
FU-12	84	70	146	NA		

a FU-x visit = posttreatment Week-x follow-up visit.
b Vital signs and hematology/chemistry safety labs will only be summarized for the FU-4 visit (up to 30 days after last dose). Coagulation and urinalysis tests are not collected at posttreatment visits.

ECG data collected at the screening visit will be listed using the nominal visit.

3.8.3. Selection of Data in the Event of Multiple Records in an Analysis Window

Depending on the statistical analysis method, single values may be required for each analysis window. For example, change from baseline by visit usually requires a single value, whereas a time-to-event analysis would not require 1 value per analysis window.

If multiple valid nonmissing numeric observations exist in an analysis window, records will be chosen based on the following rules if a single value is needed:

- For baseline, the last available record on or prior to the date of the first dose of study drug will be selected. If there are multiple records with the same time or no time recorded on the same day, the average (arithmetic mean) will be used for the baseline value.

- For postbaseline visits:

  — The record closest to the nominal day for that visit will be selected except for HCV RNA posttreatment follow-up visits, for which the latest record in the analysis window will be selected.

  — If there are 2 records that are equidistant from the nominal day, the later record will be selected.

  — If there is more than 1 record on the selected day, the average will be taken, unless otherwise specified.

- If multiple valid nonmissing categorical observations exist in a window, records will be selected as follows:

  — For baseline, the last available record on or prior to the date of the first dose of study drug will be selected. If there are multiple records with the same time or no time recorded on the same day, the value with the lowest severity will be selected (eg, normal will be selected over abnormal). If multiple ECG measurements occur on the same day prior to the first dose of any study drug, the value with the lowest severity will be selected regardless of the timing of these multiple ECG measurements.

  — For postbaseline visits, follow the same rules described above for postbaseline numeric observations, except that if there are multiple records on the same day, the most conservative value will be selected (eg, abnormal will be selected over normal).

4. SUBJECT DISPOSITION

4.1. Subject Enrollment, Screen Failures, and Disposition

4.1.1. Subject Enrollment

A summary of subjects enrolled and treated will be provided for each country and investigator within country for the "SOF/VEL 12 Weeks" group for subjects in the safety analysis set.

4.1.2. Screen Failures

Reasons for screen failure will be summarized for each screen that was performed for the study. The total number of screens and number of screen failures will be provided. Screen failures will be split into the following 2 groups:

Percentages will be calculated for the screen failure rate (denominator is number of screens), each inclusion/exclusion criteria not met (denominator is screen fails that did not meet criteria), and reasons for non-enrollment (denominator is screen fails that met eligibility criteria). A listing of reasons for screen failure will be provided, sorted by screening IDs for subjects who were screened but not treated.

4.1.3. Subject Disposition

The summary of subject disposition will be provided for "SOF/VEL 12 Weeks". The summary will present the number of subjects enrolled, and the number of subjects in each of the categories listed below.

- Treated (Safety Analysis Set)
- In FAS
- In PK Analysis Set
- Completed study treatment
- Did not complete study treatment with reasons for premature discontinuation of study treatment
- Completed study
- Did not complete the study with reasons for premature discontinuation of study

For the percentage of subjects who completed or did not complete study treatment or study, the denominator for the percentage calculation will be the total number of subjects in the Safety Analysis Set. Among subjects who completed study treatment and who discontinued study treatment, the number and percentage of subjects will be summarized for the following:

- Who had no HCV posttreatment Week 4 assessment and thereafter (No HCV FU-4 and thereafter)
- Who had HCV posttreatment Week 4 assessment but no HCV posttreatment Week 12 and thereafter (With HCV FU-4 but No FU-12 and thereafter)

If a subject did not have any HCV RNA assessment ≥ 21 days after the last dose of any study drug (ie, lower bound of FU-4 visit for HCV RNA data), the subject is categorized as having "No HCV FU-4 and thereafter." If a subject had the HCV FU-4 assessment but did not have any HCV RNA assessment ≥ 70 days after the last dose of any study drug (ie, lower bound of FU-12 visit for HCV RNA data), the subject is categorized as having "With HCV FU-4 but No FU-12 and thereafter."

In addition, the total number of subjects who were screened, enrolled, and the number of subjects in each of the disposition categories listed above will be depicted by a flowchart.

The following by-subject listings will be provided by subject identification (ID) number in ascending order to support the above summary tables:

- Disposition for subjects who complete study treatment and study
- Disposition for subjects who did not complete study treatment and/or study with reasons for premature discontinuation of study treatment and/or study
- Lot number(s)

4.2. Extent of Exposure

Extent of exposure to study drug will be examined by assessing the total duration of study drug exposure and the level of adherence to the study drug regimen specified in the protocol.

4.2.1. Duration of Exposure to Study Drug

Total duration of exposure to study drug will be defined as last dose date minus first dose date plus 1, regardless of any temporary interruptions in study drug administration, and will be expressed in weeks (ie, total duration [in days] divided by 7) using up to 1 decimal place (eg, 4.5 weeks).

The total duration of exposure to study drug (ie, weeks) will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) and using the number (ie, cumulative counts) and percentage of subjects exposed through the following time periods: Baseline (Day 1), Week 2 (Day 14), Week 4 (Day 28), Week 8 (Day 56), and Week 12 (Day 84).

A 3-day window is applied to the last planned on-treatment visit to match with the protocol-specified visit window. A summary will be provided for the "SOF/VEL 12 Weeks" group for the Safety Analysis Set.

4.2.2. Adherence to Study Drug

The total number of tablets administered will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum).

The presumed total number of tablets administered to a subject will be determined by the data collected on the drug accountability eCRF using the following formula:

$$\text{Total Number of Doses Administered} = \left(\sum \text{No. of Tablets Dispensed}\right) - \left(\sum \text{No. of Tablets Not Administered}\right)$$

The level of adherence to the study drug will be assessed based on the total amount of study drug administered relative to the total amount of study drug prescribed at baseline.

The level of adherence will be expressed in percentage using the following formula:

$$\text{Level of Adherence}(\%) = \left(\frac{\text{Total Amount of Study Drug Administered}}{\text{Total Amount of Study Drug Prescribed at Baseline}}\right) \times 100$$

Note: If calculated adherence is greater than 100%, the result will be set to 100%.

In this study, the total amount of SOF/VEL (400/100 mg) prescribed for 12 weeks would require 84 tablets.

Subjects who prematurely discontinue study drug for lack of efficacy (ie, virologic failure) will have the total amount of study drug prescribed calculated up to the first date when virologic failure criteria were met. For virologic failure confirmed by 2 consecutive measurements, the date of the first measurement will be used. If study drug bottles are dispensed on or after the date that the subject first met virologic failure criteria, these bottles will not be included in the calculation of adherence. If a bottle is dispensed and the bottle is returned empty, then the number of tablets returned will be entered as zero. If a bottle is dispensed but not returned (missing), the number of tablets taken from that bottle will be counted as zero.

Descriptive statistics for the level of adherence (n, mean, SD, median, Q1, Q3, minimum, and maximum) with the number and percentage of subjects belonging to adherence categories (eg, $< 80\%$, ≥ 80 to $< 90\%$, $\geq 90\%$) will be provided for the "SOF/VEL 12 Weeks" group for the Safety Analysis Set. No inferential statistics will be provided.

A separate by-subject listing of study drug administration and drug accountability will be provided by subject ID number (in ascending order) and visit (in chronological order).

4.3. Protocol Deviations

A summary of important protocol deviations will be provided by the Clinical Operations group for subjects in the Safety Analysis Set.

5. BASELINE CHARACTERISTICS

5.1. Demographics

Subject demographic variables (ie, age, sex, race, and ethnicity) will be summarized. Age will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum). Age categories (< 65 years, ≥ 65 years), sex, race, and ethnicity will be summarized as the number and percentage of subjects. Age is calculated in years on the date of first dose of study drug. For this study, only the year of the birthdate will be reported in eCRFs per country regulations; the month and day will be set to January 01 for purposes of calculating the subject's age. If a subject did not receive study drug after enrollment, the subject's age will be calculated from the date that the subject signed the informed consent form. The summary of demographic data will be provided for the "SOF/VEL 12 Weeks" group for the Safety Analysis Set, and by HCV Genotype and Overall for the FAS (as described in Section 3.2 of this SAP).

A by-subject demographic listing will be provided by subject ID number in ascending order.

5.2. Other Baseline Characteristics

Other baseline characteristics include:

- HCV genotype (for this study a separate table will be produced by HCV genotype and by subtype within each genotype)
- baseline body mass index (BMI; in kg/m^2) as a continuous variable and as categories (< 30 kg/m^2, ≥ 30 kg/m^2)
- IL28B (CC, non-CC; with non-CC further broken down to CT, TT)
- baseline HCV RNA (log_{10} IU/mL) as a continuous variable and as categories (< 800,000 IU/mL, ≥ 800,000 IU/mL)
- baseline ALT (U/L) as a continuous variable and as categories (≤ 1.5 × ULN, > 1.5 × ULN)
- cirrhosis (no, yes)
- baseline estimated creatinine clearance (eCrCl) using the Cockcroft-Gault equation
- prior HCV treatment (treatment-naive, treatment-experienced)
- most recent HCV treatment (DAA ± PEG + RBV, IFN ± RBV, PEG ± RBV) for treatment-experienced subjects
- most recent HCV treatment response (non-responder, relapse/breakthrough, early treatment discontinuation, unknown) for treatment-experienced subjects

- years from most recent liver transplantation on date of first dose of study drug
- prior HCV treatment experience and cirrhosis status (treatment naive with cirrhosis, treatment-experienced with cirrhosis, treatment naive without cirrhosis, treatment-experienced without cirrhosis)

Estimated creatinine clearance will be calculated by the Cockcroft-Gault method: $eCrCL_{CG}$ (mL/min) = [(140 – age (yrs)) × weight (kg) × (0.85 if female)] / (serum creatinine (mg/dL) × 72), where weight is actual weight in kilograms.

The summary of demographics and baseline characteristics will be provided for the "SOF/VEL 12 Weeks" group for the Safety Analysis Set; and overall and by HCV Genotype for the FAS (using the groupings described in Section 3.2 of this SAP). Continuous variables will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) and categorical variables using the number and percentage of subjects.

A summary of immunosuppressants administered at baseline to prevent rejection of the liver transplant will be presented for the Safety Analysis Set.

A by-subject listing of baseline characteristics will be provided by subject ID number in ascending order. The type of assay used to determine the HCV genotype (Abbott RealTime HCV genotype II assay [ie, LiPA 2.0] or Sanger NS5B population genotype and subtype and the corresponding results will also be displayed in this listing).

A separate by-subject data listing for cirrhosis determination will be provided for all subjects at screening.

A separate by-subject data listing of liver imaging results performed within 6 months of Day 1 to screen for hepatocellular carcinoma for subjects with cirrhosis will be provided.

A separate by-subject data listing for prior HCV treatment and response will be provided for all subjects who took prior HCV medications. The listing will display the prior HCV regimen and treatment, the treatment duration, and the prior HCV treatment response for treatment-experienced subjects.

5.3. Medical History

A by-subject listing of disease-specific medical history will be provided by subject ID number (in ascending order).

6. EFFICACY ANALYSES

6.1. Primary Efficacy Endpoint

6.1.1. Definition of the Primary Efficacy Endpoint

The primary efficacy endpoint is SVR12 defined as HCV RNA < LLOQ (ie, < 15 IU/mL) 12 weeks after discontinuation of the study drug in the FAS. The COBAS® AmpliPrep/COBAS® TaqMan® HCV Quantitative Test, v2.0 will be used to measure HCV RNA.

6.1.2. Statistical Hypothesis for the Primary Efficacy Endpoint

No hypothesis testing will be performed.

6.1.3. Primary Analysis of the Primary Efficacy Endpoint

The estimate of SVR12 and a 2-sided 95% exact CI based on the Clopper-Pearson method will be provided for the "SOF/VEL 12 Weeks" group {Clopper 1934}. In addition, point estimates and 95% confidence intervals will be provided by HCV genotype (as described in Section 3.2 of this SAP).

6.1.4. Subgroup Analysis of the Primary Efficacy Endpoint

Point estimates and the 2-sided 95% exact CI based on the Clopper-Pearson method will be provided for the SVR12 rate overall and by HCV genotype (1 total [and further broken down for 1a and 1b], 2, 3, 4, 5, and 6) for each subgroup outlined in Section 3.4. SVR12 rates will be summarized by categories of early viral response to explore possible early on-treatment predictors of SVR12.

6.2. Secondary Efficacy Endpoints

6.2.1. Definition of Secondary Efficacy Endpoints

Secondary efficacy endpoints include the following:

- The proportion of subjects with HCV RNA < LLOQ at 4 weeks after discontinuation of study treatment (SVR4)
- The proportion of subjects with HCV RNA < LLOQ while on treatment by study visit
- HCV RNA (log_{10} IU/mL) and change from baseline in HCV RNA (log_{10} IU/mL) by visit through end of treatment (EOT)

- The proportion of subjects with virologic failure as the following
  - — On-treatment virologic failure
    - HCV RNA ≥ LLOQ after having previously had 2 consecutive HCV RNA < LLOQ, while on treatment, confirmed with 2 consecutive values (note, second confirmation value can be posttreatment), or last available on-treatment measurement with no subsequent follow up values (ie, breakthrough)
    - > 1 $\log_{10}$IU/mL increase in HCV RNA from nadir while on treatment, confirmed with 2 consecutive values (note, second confirmation value can be posttreatment), or last available on-treatment measurement with no subsequent follow up values (ie, rebound)
    - HCV RNA persistently ≥ LLOQ through 12 weeks of treatment (ie, nonresponse)
  - — Relapse
    - HCV RNA ≥ LLOQ during the posttreatment period having achieved HCV RNA < LLOQ at EOT, confirmed with 2 consecutive values or last available posttreatment measurement
- Characterization of HCV drug resistance substitutions at baseline, during, and after therapy with SOF/VEL

6.2.2. Analysis Methods for Secondary Efficacy Endpoints

For analyses of HCV RNA < LLOQ by visit while on treatment and during the posttreatment (SVR) follow-up period, subjects will be assigned a value at each visit based on the analysis visit windows specified in Section 3.8.2. Missing values will be imputed based on the categorical imputation rules described in Section 3.6.1. The 2-sided 95% exact CI based on the Clopper-Pearson method will be provided for the proportion of subjects with HCV RNA < LLOQ at each visit for "SOF/VEL 12 Weeks" and by HCV genotype (1 total [and further broken down for 1a and 1b], 2, 3, 4, 5, and 6). The overall category for "HCV RNA < LLOQ" will be split into the following 2 subcategories: "< LLOQ TND" for subjects with target not detected and "< LLOQ detected" for subjects with < LLOQ in tabular displays.

Summary statistics will be presented for absolute values and change from baseline in HCV RNA ($\log_{10}$ IU/mL) by visit through the end of treatment. Imputation rules described in Section 3.6.1 will be used to assign HCV RNA values for missing values at a visit that are bracketed by "< LLOQ TND" and/or "< LLOQ detected". Otherwise, a missing = excluded analysis will be performed. Plots of the mean ± SD and median (Q1, Q3) of absolute values and changes from baseline in HCV RNA through EOT will be presented for "SOF/VEL 12 Weeks" and by HCV genotype (1 total [and further broken down for 1a and 1b], 2, 3, 4, 5, and 6) according to the rules specified above.

For the SVR12 endpoint analysis, a summary table of the number and proportion of subjects with SVR12, virologic failure, and Other will be created. All subjects who achieve SVR12 will be categorized as SVR12. Virologic failure will be descriptively summarized as "on-treatment virologic failure" and relapse (which will be broken down by study drug completed yes/no). Subjects who do not achieve SVR12 and do not meet criteria for virologic failure will be categorized as Other. The denominator for relapse will be the number of subjects who had HCV RNA < LLOQ on their last observed on-treatment HCV RNA measurement; otherwise, the denominator will be the number of subjects in the FAS. Virologic outcomes will be provided for "SOF/VEL 12 Weeks" and by HCV genotype (1 total [and further broken down for 1a and 1b], 2, 3, 4, 5, and 6 as described above. Separate listings will be provided for subjects with virologic failure and for subjects who meet the criteria for "Other".

In addition, a summary table of the number and proportion of subjects with HCV RNA < LLOQ and ≥ LLOQ at the posttreatment follow-up visit (observed and imputed, with reasons for imputation) will be provided for each posttreatment follow-up visit. Results will be displayed for "SOF/VEL 12 Weeks" and by HCV genotype (1 total [and further broken down for 1a and 1b], 2, 3, 4, 5, and 6). The 2-sided 95% Clopper-Pearson exact CIs will be presented for the proportion of subjects with HCV RNA < LLOQ.

Drug resistant substitutions will be analyzed as part of a separate Virology Study Report.

6.3. Exploratory Efficacy Endpoints

6.3.1. Definition of Exploratory Efficacy Endpoints

PPD

6.4. Changes From Protocol-Specified Efficacy Analyses

There are no planned changes from protocol-specified efficacy analyses.

7. SAFETY ANALYSES

7.1. Adverse Events and Deaths

7.1.1. Adverse Event Dictionary

Clinical and laboratory adverse events (AEs) will be coded using the current version of MedDRA. System organ class (SOC), high level group term (HLGT), high level term (HLT), preferred term (PT), and lower level term (LLT) will be provided in the AE dataset.

7.1.2. Adverse Event Severity

Adverse events are graded by the investigator as Grade 1, 2, 3, or 4 using the Gilead Grading Scale for Severity of Adverse Events and Laboratory Abnormalities. The severity grade of events for which the investigator did not record severity will be categorized as "missing" for tabular summaries and data listings, and the most severe will be considered (for sorting purpose only) in data presentation.

7.1.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected "Related" on the AE eCRF to the question of "Related to Study Treatment." Events for which the investigator did not record the relationship to study drug will be considered to be related to study drug for summary purposes. However, by-subject data listings will show the relationship as missing from that captured on the eCRF.

7.1.4. Serious Adverse Events

Serious adverse events (SAEs) will be identified and captured as SAEs if AEs met the definitions of SAE specified in the study protocol. Serious adverse events captured and stored in the clinical database will be reconciled with the SAE database from the Gilead Drug Safety and Public Health Department before database finalization.

7.1.5. Treatment-Emergent Adverse Events

7.1.5.1. Definition of Treatment-Emergent

Treatment-emergent adverse events (TEAEs) are defined as one or both of the following:

- Any AEs with an onset date on or after the study drug start date and no later than 30 days after permanent discontinuation of study drug
- Any AEs leading to premature discontinuation of study drug.

7.1.5.2. Incomplete Dates

If the onset date of an AE is incomplete, then the month and year (or year alone if month is not recorded) of onset determine whether an AE is treatment emergent, as long as the AE stop date is not prior to the first dose date of study drug. The event is considered treatment emergent if both of the following 2 criteria are met:

- The AE onset and end dates are the same as or after the month and year (or year) of the first dose date of study drug
- The AE onset date is the same as or before the month and year (or year) of 30th day after the date of the last dose of study drug

An AE with completely missing onset and stop dates, or with the onset date missing and a stop date later than the first dose date of study drug, will be considered to be treatment-emergent.

7.1.6. Summaries of Adverse Events and Deaths

A brief high-level summary of TEAEs will be provided for the "SOF/VEL 12 Weeks" group for the number and percentage of subjects who had the following: any AE, any AE of Grade 3 or above, any AE of Grade 2 or above, any treatment-related AE, any treatment-related AE of Grade 3 or above, any treatment-related AE of Grade 2 or above, any SAE, any treatment-related SAE, any AE that led to premature discontinuation of SOF/VEL, any AE that led to interruption of SOF/VEL. All deaths (including those that are treatment emergent and those that are not treatment emergent) observed during the study will also be summarized and included in this table.

Adverse event summaries will provide the number and percentage of subjects with TEAEs by SOC and PT, for the "SOF/VEL 12 Weeks" group based on the Safety Analysis Set as follows:

- All AEs
- AEs of Grade 3 or above
- AEs of Grade 2 or above
- All treatment-related AEs
- Treatment-related AEs of Grade 3 or above
- Treatment-related AEs of Grade 2 or above
- All SAEs
- All treatment-related SAEs

Multiple events will be counted once only per subject in each summary. Adverse events will be summarized and listed first in alphabetic order of SOC and then by PT in order of descending incidence within each SOC. In summaries by severity grade, the most severe grade will be used for those AEs that occurred more than once in an individual subject during the study.

In addition to the above summary tables, TEAEs will be summarized by PT only, in order of descending incidence for:

- AEs that occurred in at least 5% of subjects within any treatment group
- AEs of Grade 3 or above
- AEs related to study drug
- All SAEs
- AEs leading to premature discontinuation of study drug
- AEs leading to interruption of study drug

In addition to the summaries described above, data listings will be provided for the following:

- All AEs (with a variable indicating whether the event is treatment emergent)
- AEs of Grade 3 or above
- SAEs
- Deaths
- AEs leading to premature discontinuation of study drug

7.2. Laboratory Evaluations

Laboratory data collected during the study will be summarized using both quantitative and qualitative methods. Summaries of laboratory data will be provided for the Safety Analysis Set and will include data collected up to the last dose date of study drug plus 30 days. The analysis will be based on values reported in conventional units. When values are below the limit of quantitation, they will be listed as such, and the closest imputed value will be used for the purpose of calculating summary statistics. For example, if "< 50" was recorded, a value of 49 will be used for the purpose of calculating summary statistics; if "< 0.1" was recorded, a value of 0.09 will be used for the purpose of calculating summary statistics. Hemolyzed test results will not be included in the analysis, but they will be listed in by-subject laboratory listings.

For this study, an enzymatic serum creatinine test was used (reflex test) when the sample was icteric and serum creatinine level could not be determined by the central laboratory. Results from

the enzymatic serum creatinine test will be used in place of a missing serum creatinine value per the standard methodology, when appropriate. Covance Laboratories has conducted correlation testing to show that the results of these 2 tests are similar and can be pooled for analysis.

A by-subject listing for laboratory test results will be provided by subject ID number and visit in chronological order for hematology, serum chemistry, and urinalysis separately. Values falling outside of the relevant reference range and/or having a severity grade of 1 or higher on the Gilead Grading Scale for Severity of Adverse Events and Laboratory Abnormalities will be flagged in the data listings, as appropriate.

No inferential statistics will be generated.

7.2.1. Summaries of Numeric Laboratory Results

Descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) will be provided for the "SOF/VEL 12 Weeks" group for ALT, aspartate transaminase (AST), total bilirubin, alkaline phosphatase, hemoglobin, reticulocytes, white blood cells (WBC), neutrophils, lymphocytes, platelets, and international normalized ratio (INR) as follows:

- Baseline values
- Values at each postbaseline visit
- Change from baseline at each postbaseline visit

A baseline laboratory value will be defined as the final assessment performed on or prior to the date of first dose of study drug. Change from baseline to a postbaseline visit will be defined as the visit value minus the baseline value. The mean, median, Q1, Q3, minimum, and maximum will be displayed to reported number of digits, SD to reported number of digits plus 1.

Median (Q1, Q3) of the observed values for ALT, AST, total bilirubin, alkaline phosphatase, hemoglobin, reticulocytes, WBC, neutrophils, lymphocytes, and platelets will be plotted using a line plot for the "SOF/VEL 12 Weeks" group by visit.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.8.3 (Selection of Data in the Event of Multiple Records in a Window).

The percentage of subjects with at least 1 postbaseline (up to 30 days post last dose) hemoglobin value < 10 g/dL and < 8.5 g/dL will be summarized for the "SOF/VEL 12 Weeks" group. The denominator will be the number of subjects with at least 1 postbaseline hemoglobin value. Note that a subject with a minimum hemoglobin value on treatment of 8.3 g/dL would be counted in both categories.

A listing of subjects meeting the criteria for postbaseline hemoglobin < 10 g/dL and < 8.5 g/dL will be provided.

7.2.2. Graded Laboratory Values

The Gilead Grading Scale for Severity of Adverse Events and Laboratory Abnormalities will be used for assigning toxicity grades (0 to 4) to laboratory results for analysis. Grade 0 includes all values that do not meet the criteria for an abnormality of at least Grade 1. Some laboratory tests have criteria for both increased and decreased levels; analyses for each direction (ie, increased, decreased) will be presented separately.

7.2.2.1. Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point, up to and including the date of last dose of study drug plus 30 days. If the relevant baseline laboratory value is missing, then any abnormality of at least Grade 1 will be considered treatment emergent.

7.2.2.2. Summaries of Laboratory Abnormalities

Laboratory data that are categorical will be summarized using the number and percentage of subjects in the study with the given response at baseline and each scheduled postbaseline visit.

The following summaries (number and percentage of subjects) for treatment-emergent laboratory abnormalities will be provided for the "SOF/VEL 12 Weeks" group by analyte; subjects will be categorized according to the most severe postbaseline abnormality grade for a given analyte:

- Graded laboratory abnormalities
- Grade 3 or above laboratory abnormalities

For all summaries of laboratory abnormalities, the denominator is the number of subjects with nonmissing postbaseline values up to 30 days after last dose for the laboratory parameter of interest.

A by-subject listing of treatment-emergent Grade 3 or above laboratory abnormalities will be provided by subject ID number and visit in chronological order. This listing will include all test results that were collected throughout the study for the analyte of interest, with all applicable severity grades or abnormal flags displayed. By-subject listings of laboratory data will be provided by subject ID number and visit in chronological order.

7.3. Body Weight, Height, and Vital Signs

Vital signs (systolic and diastolic blood pressure [mmHg], and pulse [beats/min]) at each visit, and change from baseline at each visit will be summarized for the Safety Analysis Set using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, and maximum) for the "SOF/VEL 12 Weeks" group. The baseline value will be defined as the last available value collected on or prior to the date of first dose of study drug. Change from baseline to a postbaseline visit will be defined as the postbaseline value minus the baseline value.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.8.3 (Selection of Data in the Event of Multiple Records in a Window). No inferential statistics will be generated.

A by-subject listing of body weight, height, BMI, and vital signs (systolic and diastolic blood pressure [mmHg], pulse [beats/min], respiration [breaths/min], and body temperature [°C]) will be provided by subject ID number and visit in chronological order.

7.4. Prior and Concomitant Medications

Medications collected at screening and during the study will be coded using the current version of the World Health Organization (WHO) Drug dictionary. The medications will be categorized as prior or concomitant using the following definitions:

- Prior medications: any medications taken and stopped prior to or on the date of first study drug administration

- Concomitant medications: any medications taken after the date of first study drug administration and up to the last dosing date of the study drug

Concomitant medications (other than study drug and drugs administered to prevent rejection of the transplanted organ) will be summarized by Anatomical Therapeutic Chemical (ATC) drug class Level 2, and preferred name using the number and percentage of subjects for the "SOF/VEL 12 Weeks" group. A subject reporting the same medication more than once will be counted only once when calculating the number and percentage of subjects who received that medication. The summary of concomitant medications will be ordered alphabetically by ATC drug class and then by descending frequency of preferred names within an ATC drug class. For drugs with the same frequency, sorting of preferred names will be done alphabetically.

Summaries will be based on the Safety Analysis Set. No inferential statistics will be generated.

For purposes of analysis, any medication with a stop date that is on or prior to the initial study drug dosing date or start date that is after the last study drug dosing date will be excluded from a concomitant medication summary. If a partial stop date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) prior to the initial study drug dosing date will be excluded from the concomitant medication summary. If a partial start date is entered, then any medication with the month and year (if day is missing) or year (if day and month are missing) after the study drug stop date will be excluded from the concomitant medication summary. Medications with completely missing dates will be included in the concomitant medication summary.

All prior and concomitant medications (other than per-protocol study drugs and immunosuppressants given to prevent rejection of the transplanted liver) will be provided in a by-subject listing sorted by subject ID number and administration date in chronological order.

7.5. Concomitant Immunosuppressants

Immunosuppressant medications administered to prevent rejection of the transplanted liver will be summarized separately by Anatomical Therapeutic Chemical (ATC) drug class Level 2, and preferred name. The WHO preferred name and drug code will be attached to the clinical database. Immunosuppressants taken while the subject is receiving study drug will be summarized by WHO drug class and generic name. Definitions for concomitant medications and imputations for partial dates are as described for concomitant medications. The summary of concomitant immunosuppressant medications will be ordered alphabetically by ATC drug class and then by descending frequency of preferred names within an ATC drug class.

The number and percentage of subjects with any change in concomitant immunosuppressant medication will be summarized overall by reason for change (drug-drug interaction [DDI], protocol defined change [PDC], improvement in organ function [IOF], renal insufficiency [RIS], failing graft [FGR], and other [OTH]). The denominator for percentage calculation is the number of subjects taking any concomitant immunosuppressant for the safety analysis set. Similarly, for each drug class, the number and percentage of subjects with a dose change will be summarized by reason for change (denominator will be number of subjects receiving a concomitant drug in that class). The classes will be calcineurin inhibitors (ciclosporin, tacrolimus), rapamycin inhibitors (sirolimus, everolimus), purine/pyrimidine synthesis inhibitors (mycophenolate and its derivatives), antimetabolites (azathioprine), and corticosteroids (prednisone, prednisolone, methylprednisolone). A subject may have more than 1 reason for change recorded, and may appear in more than 1 change category.

A listing of immunosuppressant drugs administered to subjects will be provided, including the reason for any dose modification. If suspected drug-drug interaction is the reason marked for a dose change, whether the drug-drug interaction was confirmed will be included.

For subjects who take calcineurin or mTOR inhibitors (a class of drugs that inhibit the mechanistic target of rampamycin) and have blood concentrations collected, a listing will be provided. This listing will be sorted by subject ID, calcineurin or mTOR inhibitor name, and date of collection for the blood sample.

7.6. Investigator Electrocardiogram Assessment

A by-subject listing for ECG assessment results at screening will be provided by subject ID number. A separate listing will be provided for subjects with clinically significant ECG abnormalities.

7.7. Other Safety Measures

A listing of pregnancies and rejection episodes will be provided.

7.8. Changes From Protocol-Specified Safety Analyses

There are no deviations from the protocol-specified safety analyses.

8. PHARMACOKINETIC ANALYSES

The plasma concentrations of SOF and its metabolites GS-566500 and GS-331007, and VEL will be determined using validated bioanalytical assays.

For all subjects, a single PK blood sample will be collected at any time for each on-treatment visit except for Study Day 1.

Population PK models for SOF, GS-331007, and VEL previously developed for regulatory submission may be applied to the data of this study. PK parameters (AUC_{tau} and C_{max} of SOF and GS-331007, and AUC_{tau}, C_{max}, and C_{tau} for VEL) may be estimated for the simulated SOF, GS-331007, and VEL concentration data using respective population PK models. The drug concentrations and population PK model-derived PK parameters for SOF, GS-331007, and VEL will be listed, as appropriate.

9. REFERENCES

Clopper CJ, Pearson ES. The Use of Confidence or Fiducial Limits Illustrated in the Case of the Binomial. Dec. Biometrika 1934;26 (4):pp. 404-13.

10. SOFTWARE

SAS® Software Version 9.2. SAS Institute Inc., Cary, NC, USA.

11. SAP REVISION

Revision Date (DD MMM YYYY)	Section	Summary of Revision	Reason for Revision

12. APPENDICES

Appendix 1. Table of Contents for Statistical Tables, Figures, and Listings

Appendix 1. Table of Contents for Statistical Tables, Figures, and Listings

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15.8.3.2*	Demographics and Baseline Characteristics by HCV Genotype and Overall	Full Analysis Set
15.8.3.3	HCV Genotype and Subtype	Safety Analysis Set
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15.11.2.1.3	Treatment-Emergent Adverse Events That Occurred in At Least 5% of Subjects by Preferred Term	Safety Analysis Set
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15.11.2.3.3	Treatment-Emergent Treatment-Related Adverse Events of Grade 3 or Above	Safety Analysis Set
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Table Number	Title	Analysis Set
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15.11.6.1.1	ALT (U/L) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.1.2	AST (U/L) and Change from Baseline by Visit	Safety Analysis Set
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* Groups are SOF/VEL 12 Weeks; and by HCV GT (1 Total, 1a, 1b, 2, 3, 4, 5, and 6).

Figure Number	Title	Analysis Set
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Listing Number	Title	Analysis Set
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16.2.2.2	Subjects Enrolled and Treated Who Did Not Meet Eligibility Criteria	Safety Analysis Set
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16.2.5.2	Study Drug Accountability and Adherence	Safety Analysis Set
16.2.5.3	Plasma PK Sampling Details and PK Concentrations	PK Analysis Set
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16.2.8.1.4.1	Screen Labs: HBsAg, Anti-HIV Ab, Anti-HCV Ab, HbA1c, and Serum Beta hCG	Safety Analysis Set
16.2.8.1.4.2	Drugs of Abuse Screen: Amphetamines/MDMA, Cocaine, Methadone, and Opiates	Safety Analysis Set
16.2.8.1.5.1	Hematology: Hematocrit, Hemoglobin, Reticulocytes, MCV, RBC, WBC, and Platelets	Safety Analysis Set
16.2.8.1.5.2	Hematology: WBC, Neutrophils, and Lymphocytes	Safety Analysis Set
16.2.8.1.5.3	Hematology: Eosinophils, Basophils, and Monocytes	Safety Analysis Set
16.2.8.1.6	Coagulation: INR and APTT	Safety Analysis Set
16.2.8.1.7.1	Serum Chemistry: Sodium, Potassium, Bicarbonate, Phosphorus, and Uric Acid	Safety Analysis Set
16.2.8.1.7.2	Serum Chemistry: AST, ALT, Total Bilirubin, Direct Bilirubin, Alkaline Phosphatase, GGT, Albumin, and Lipase	Safety Analysis Set
16.2.8.1.7.3	Serum Chemistry: Creatine Kinase, Creatinine, Estimated Creatinine Clearance (Cockcroft-Gault), and Glucose	Safety Analysis Set
16.2.8.1.8.1	Urinalysis: Urine Blood, Glucose, pH, Protein, Urobilinogen, and Leukocyte Esterase	Safety Analysis Set
16.2.8.1.8.2	Microscopic Urinalysis for Subjects with Abnormal Macroscopic Urinalysis	Safety Analysis Set
16.2.8.2.1	Height, Weight, BMI, and Vital Signs	Safety Analysis Set
16.2.8.2.2.1	12-Lead Electrocardiogram Results	Safety Analysis Set
16.2.8.2.2.2	12-Lead Electrocardiogram Results for Subjects with Clinically Significant Abnormalities	Safety Analysis Set
16.2.8.3	Pregnancy	Safety Analysis Set
16.2.8.4	Subjects with Acute Rejection Episodes	Safety Analysis Set