STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 2b, Open-Label Study of 200 mg or 400 mg Sofosbuvir+RBV for 24 Weeks in Genotype 1 or 3 and Ledipasvir/Sofosbuvir (LDV/SOF) Fixed-Dose Combination (FDC) Tablet for 12 weeks in Genotype 1 or 4 HCV-Infected Subjects with Renal Insufficiency
Name of Test Drug:	Sofosbuvir, Ledipasvir/Sofosbuvir Fixed-Dose Combination
Study Number:	GS-US-334-0154 (Cohort 3)
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Analysis Type:	SVR12 and Final Analysis for Cohort 3
Analysis Plan Version:	Version 1
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Analysis Plan Author(s):	PPD

CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BLQ	below the limit of quantitation
BMI	body mass index
CI	confidence interval
CK	creatine kinase
CRF	case report form
CSR	clinical study report
ECG	electrocardiogram
eCRF	electronic case report form
eGFR	estimated glomerular filtration rate
ET	early termination
FAS	Full Analysis Set
FU	follow-up
HCV	hepatitis C virus
HLGT	high-level group term
HLT	high-level term
IBW	ideal body weight
INR	international normalized ratio
IL28B	IL28B gene
LDV	ledipasvir, GS-5885
LLOQ	lower limit of quantitation
LLT	lower level term
MedDRA	Medical Dictionary for Regulatory Activities
nadir	the lowest point
PK	pharmacokinetic
PT	preferred term
Q1, Q3	first quartile, third quartile
RNA	ribonucleic acid
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SOC	system organ class
SOF	sofosbuvir, GS-7977
SVR	sustained virologic response
TEAE	treatment-emergent adverse event
TFLs	tables, figures, and listings

TND	target not detected
ULN	upper limit of normal
VF	virologic failure
WHO	World Health Organization

PHARMACOKINETIC ABBREVIATIONS

AUC_{last}	area under the concentration versus time curve from time zero to the last quantifiable concentration
AUC_{tau}	area under the concentration versus time curve over the dosing interval
C_{last}	last observed quantifiable concentration of the drug
C_{max}	maximum observed concentration of drug
C_{tau}	observed drug concentration at the end of the dosing interval
$t_{1/2}$	estimate of the terminal elimination half-life of the drug, calculated by dividing the natural log of 2 by the terminal elimination rate constant (λ_z)
T_{last}	time (observed time point) of C_{last}
T_{max}	time (observed time point) of C_{max}
λz	terminal elimination rate constant, estimated by linear regression of the terminal elimination phase of the concentration of drug versus time curve

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 Cohort 3 from Study GS-US-334-0154. A separate SAP for Cohorts 1 and 2 was finalized on 05 February 2016, and the CSR for Cohorts 1 and 2 was approved on 26 May 2016. The current SAP is based on the study protocol Amendment 4 dated 23 April 2015 and the electronic case report form (eCRF), and will only present the plan for statistical analyses of Cohort 3 of this study. The SAP will be finalized before SVR12 analysis database finalization. Any changes made after the finalization of the SAP will be documented in the CSR.

1.1. Study Objectives

The primary objective of cohort 3 in this study are as follows:

- To evaluate the safety of LDV/SOF for 12 weeks as assessed by review of the accumulated safety data
- To evaluate the efficacy of LDV/SOF for 12 weeks measured by the proportion of subjects with renal insufficiency who have achieved a sustained viral response 12 weeks after treatment discontinuation (SVR12)
- To evaluate the steady state pharmacokinetics of SOF and its metabolites and LDV upon dosing LDV/SOF in subjects with renal insufficiency

The secondary objectives of cohort 3 in this study are as follows:

- To evaluate the proportion of subjects with renal insufficiency who attain SVR at 4 and 24 weeks after discontinuation of treatment (SVR4 and SVR24)
- To evaluate the kinetics of plasma HCV RNA during and after treatment discontinuation
- To evaluate the emergence of viral resistance to SOF and LDV during and after treatment discontinuation

The exploratory objective of cohort 3 in this study is:

PPD

1.2. Study Design

This is a multicenter, open-label study cohort that will evaluate the safety, tolerability, and antiviral efficacy of LDV/ SOF in subjects with chronic renal insufficiency and genotype 1 or 4 HCV infection, including subjects with compensated cirrhosis.

Approximately 35subjects with severe renal insufficiency will be enrolled as below.

- Cohort 1: 10 subjects will receive SOF 200 mg + RBV 200 mg once daily for 24 weeks.
- Cohort 2: Following review of safety, efficacy and pharmacokinetic (PK) data through post-treatment Week 4 of Cohort 1, 10 additional subjects will receive SOF 400mg + RBV 200mg once daily for 24 weeks.
- Cohort 3: Following review of safety and available PK data through Week 12 of Cohort 2, 15 additional subjects will receive LDV/SOF once daily for 12 weeks.

The total time to complete all study visits in Cohort 3 is approximately 42 weeks including the following periods:

- Up to 42-day (6-week) screening period
- 12-week treatment period
- Up to 24-week posttreatment period

The schedule of assessments is provided as an appendix to the SAP (Appendix 1).

1.3. Sample Size and Power

Due to the exploratory nature of this study, no formal power or sample size calculations were performed to determine treatment group size. The total sample size of 35 is largely based on feasibility.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analyses

2.1.1. SVR12 Analysis

The analysis for the primary endpoint SVR12 will occur after all subjects complete the posttreatment Week 12 visit or prematurely discontinue from the study. All safety and efficacy data through the posttreatment Week 12 visit will be cleaned, finalized and included in the analysis.

2.2. Final Analysis

After all subjects have completed the study or early terminated the study, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have 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) or standard error (SE), median, first quartile (Q1), third quartile (Q3), minimum, and maximum will be presented.

By-subject listings will be presented for all subjects in the All Enrolled Analysis Set and sorted by subject ID number, visit date, and time (if applicable). Data collected on log forms, such as AEs, will be presented in chronological order within the subject. Age, sex at birth, race, and ethnicity will be included in the listings, as space permits.

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 analysis set will be identified and included as a subtitle of each table, figure, and listing.

For each analysis set, the number and percentage of subjects eligible for inclusion, as well as the number and percentage of subjects who were excluded (if any), will be summarized.

3.1.1. All Enrolled Analysis Set

All Enrolled Analysis Set includes all subjects who received a study subject identification number in the study after screening.

3.1.2. Full Analysis Set

The Full Analysis Set (FAS) includes all subjects who were enrolled and took at least 1 dose of study drug. The study drug for Cohort 3 in this study is LDV/SOF. 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 study drug. This is the primary analysis set for safety analyses.

3.1.4. Pharmacokinetic Analysis Set

The Pharmacokinetic (PK) Analysis Set will include all enrolled subjects who took at least 1 dose of study drug and have at least 1 nonmissing postdose concentration value reported by the PK laboratory. This is the primary analysis set for all PK analyses.

3.2. Subject Grouping

In Cohort 3 of this study, there is only 1 treatment, which is LDV/SOF once daily for 12 weeks. Therefore, for all analysis sets, there will be only 1 group.

3.3. Strata and Covariates

This study does not use a stratified randomization schedule when enrolling subjects.
No covariates will be included in efficacy and safety analyses.

3.4. Examination of Subject Subgroups

There are no prespecified subject subgroupings for efficacy analyses.

3.5. Multiple Comparisons

Adjustments for multiplicity will not be made, because no formal statistical testing will be performed in this study.

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. Exceptions are presented in this document.

For missing last dosing date of study drug, imputation rules are described in Section 4.2.1. The handling of missing or incomplete dates for AE onset is described in Section 7.1.5.2, and for prior and concomitant medications in Section 7.3.

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 the 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 is greater than or equal to the lower bound of a visit window, and the value at the visit is missing, 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 "< lower limit of quantification (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) except for SVR24, which will be imputed according to SVR12 status. Success for SVR12 for subjects who have no further HCV RNA measurements collected will be counted as a success for SVR24 due to the high correlation between these 2 endpoints.

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 rule described above, the corresponding continuous value will 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

In general, age (in years) on the date of the first dose of study drug will be used for analyses and presentation in listings. If an enrolled subject was not dosed with any study drug, the enrollment date will be used instead of the first dosing date of study drug. For screen failures, the date the informed consent was signed will be used for age calculation. If only the birth year is collected on the CRF, "01 July" will be used for the unknown birth day and month for the purpose of age calculation. If only birth year and month are collected, "01" will be used for the unknown birth day.

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

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

- A value that is 1 unit above the LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "> x" (where x is considered the LOQ). Values with decimal points will follow the same logic as above.

- The LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "≤ x" or "≥ x" (where x is considered the LOQ).

The COBAS®AmpliPrep/COBAS® TaqMan® HCV Quantitative Test v2.0 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 reported as the "<< numeric value>> IU/mL". This result will be referred to in this document as the numeric result or as "≥ LLOQ detected" for 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.

For selected analyses, HCV RNA data (IU/mL) will be transformed to the logarithmic (base 10) scale ($\log_{10}$ IU/mL).

Natural logarithm transformation will be used for plasma/blood concentrations and analysis of PK parameters. Plasma concentration values that are below the limit of quantitation (BLQ) will be presented as "BLQ" in the concentration data listing. Values that are BLQ will be treated as 0 at predose time points, and one-half the value of the limit of quantitation (LOQ) at postbaseline time points for determination of summary and order statistics.

The following conventions will be used for the presentation of summary and order statistics:

- If at least 1 subject has a concentration value of BLQ for the time point, the minimum value will be displayed as "BLQ."
- If more than 25% of the subjects have a concentration data value of BLQ for a given time point, the minimum and Q1 values will be displayed as "BLQ."
- If more than 50% of the subjects have a concentration data value of BLQ for a given time point, the minimum, Q1, and median values will be displayed as "BLQ."
- If more than 75% of the subjects have a concentration data value of BLQ for a given time point, the minimum, Q1, median, and Q3 values will be displayed as "BLQ."
- If all subjects have concentration data values of BLQ for a given time point, all order statistics (minimum, Q1, median, Q3, and maximum) will be displayed as "BLQ."

Exposure parameters selected for statistical analysis will be natural log-transformed. PK parameters that are BLQ will be imputed as one-half LOQ before log transformation or statistical model fitting.

3.8. Analysis Visit Windows

3.8.1. Definition of Study Day

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

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

Therefore, Study Day 1 is the day of first dose of study drug administration.

The last dose date for an individual 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 Visit Windows

Subject visits might not occur on protocol-specified days. Therefore, for the purpose of analysis, observations will be assigned to analysis windows. Analysis windows are defined for HCV RNA, vital signs, safety laboratory, and electrocardiogram (ECG).

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, safety laboratory and ECG data collected up to the last dose date + 2 days are considered to be on-treatment data and HCV RNA, vital signs, safety laboratory and ECG data collected after the last dose date + 2 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. The analysis windows for on-treatment ECG data are provided in Table 3-2.

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

Nominal Visit	Nominal Day	Lower Limit	Upper Limit
Baseline	1	(none)	1
Week 1	7	2	11
Week 2	14	12	21
Week 4	28	22	35
Week 6	42	36	49
Week 8	56	50	63
Week 10	70	64	77
Week 12	84	78	≥ 85

Table 3-2. Analysis Windows for On-treatment ECG Data

Nominal Visit	Nominal Day	Lower Limit	Upper Limit
Baseline	1	(none)	1
Week 4	28	2	42
Week 8	56	43	70
Week 12	84	71	≥ 85

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

Table 3-3. Analysis Windows for Posttreatment HCV RNA, Vital Signs, Safety Laboratory and ECG Data

	HCV RNA			Vital Signs, Safety Laboratory and ECG 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	3	30
FU-12	84	70	146	NA		
FU-24	168	147	190	NA		

a FU-x visit = posttreatment Week-x follow-up visit.
b Vital signs and safety laboratory data will be summarized only for the FU-4 visit (up to 30 days after last dose).

3.8.3. Selection of Data in the Event of Multiple Records in an Analysis Visit 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, continuous measurements exist in an analysis window, records will be chosen based on the following rules if a single value is needed:

- In general, the baseline value will be the last nonmissing value on or prior to the first dosing date of study drug, unless specified differently. If multiple measurements occur on the same day, the last nonmissing value prior to the time of first dosing of study drug will be considered as the baseline value. If these multiple measurements occur at the same time or the time is not available, the average of these measurements (for continuous data) will be considered the baseline value.

- For postbaseline values:

  – The record closest to the nominal day for that visit 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 measurements 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 value with the lowest severity will be selected (eg, normal will be selected over abnormal for safety ECG findings).

- For postbaseline visits, if there are multiple records with the same time or no time recorded on the same day, the value with the worst severity within the window will be selected (eg, abnormal will be selected over normal for safety ECG findings).

4. SUBJECT DISPOSITION

4.1. Subject Enrollment and Disposition

A summary of subject enrollment will be provided for each country and for each investigator within a country, and overall. The summary will present the number and percentage of subjects enrolled. The denominator for the percentage calculation will be the total number of subjects in the Safety Analysis Set.

A summary of subject disposition will be provided. This summary will present the number of subjects screened, the number of subjects not enrolled, the number of subjects enrolled, and the number of subjects in each of the categories listed below:

- Safety Analysis Set
- FAS
- PK Analysis Set
- Completed study drug
- Did not complete study drug with reasons for premature discontinuation of study drug
- Completed study
- Did not complete the study with reasons for premature discontinuation of study

For the status of study drug and study completion and reasons for premature discontinuation, the number and percentage of subjects in each category will be provided. The denominator for the percentage calculation will be the total number of subjects in the Safety Analysis Set. Among subjects who completed study drug and who discontinued study drug, 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 assessment 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 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 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, a flowchart will be provided to depict the disposition.

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

- Subject disposition
- Reasons for screen failure (will be provided by screening ID number in ascending order)
- Lot number and kit ID

4.2. Extent of Study Drug Exposure and Adherence

Extent of exposure to study drug will be examined by assessing the total duration of exposure to study drug and the level of adherence to study drug 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 dosing date minus first dosing date plus 1, regardless of any temporary interruptions in study drug administration, and will be expressed in weeks using up to 1 decimal place (eg, 4.5 weeks). If the last study drug dosing date is missing, the latest date among the study drug end date, clinical visit date, laboratory sample collection date, and vital signs assessment date that occurred during the on-treatment period will be used.

The total duration of exposure to study drug will be summarized using descriptive statistics and using the number (ie, cumulative counts) and percentage of subjects exposed through the following time periods: Baseline (Day 1), Week 1 (Day 7), Week 2 (Day 14), Week 4 (Day 28), Week 8 (Day 56), and Week 12 (Day 84).

Summaries will be provided for the Safety Analysis Set.

No formal statistical testing is planned.

4.2.2. Adherence to Study Drug

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

Total Number of Doses Administered =

$$\left(\sum \text{No. of Doses Dispensed}\right) - \left(\sum \text{No. of Doses Returned}\right)$$

If there are study drug bottles dispensed on or after 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.

The level of prescribed adherence to study drug will be determined by the total amount of study drug administered relative to the total amount of study drug specified by the protocol for a subject who completes treatment in the study.

The level of prescribed adherence will be expressed as a percentage using the following formula:

$$\text{Prescribed Adherence (\%)} = \left(\frac{\text{Total Amount of Study Drug Administered}}{\text{Total Amount of Study Drug Specified by Protocol}} \right) \text{x } 100$$

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

In this study, the total amount of LDV/SOF prescribed for 12 weeks of treatment would require 84 doses. 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.

Descriptive statistics for the level of prescribed adherence with the number and percentage of subjects belonging to adherence categories (eg, $< 80\%$, ≥ 80 to $< 90\%$, $\geq 90\%$) will be provided for the Safety Analysis Set.

No formal statistical testing is planned.

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

4.3. Protocol Deviations

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

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

The following subject demographic and baseline characteristics will be summarized by treatment cohort and overall using descriptive statistics (n, mean, standard deviation, median, Q1, Q3, minimum and maximum) for continuous data and by the number and percent of subjects for categorical data. Variables to be summarized include the following:

- age (on date of first dose of any study drug) as a continuous variable
- sex at birth (male, female)
- race
- ethnicity (hispanic or latino, not hispanic or latino)
- body weight (in kg)
- height (in cm)
- body mass index (BMI; in kg/m^2) as a continuous variable and as categories (< 30 kg/m^2, ≥ 30 kg/m^2)
- HCV genotype
- cirrhosis (presence, absence)
- 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 (< 6 log_{10} IU/mL, ≥ 6 log_{10} IU/mL)
- baseline ALT as a continuous variable and as categories categories ($\leq 1.5 \times$ ULN, $> 1.5 \times$ ULN)
- estimated glomerular filtration rate (eGFR) using the Cockcroft-Gault equation
- prior HCV treatment experience (treatment naive, treatment experienced)
- prior HCV treatment response for treatment-experienced subjects
- most recent HCV treatment regimen for treatment-experienced subjects
- fibrotest score as a continuous variable and fibrotest stage as a categorical variable

Age is calculated as the integer of age in years at first dose of study regimen.

eGFR will be calculated by the Cockcroft-Gault method using ideal body weight (IBW): $eGFR_{CG}$ (mL/min) = [(140 – age (yrs)) × IBW (kg) × (0.85 if female)] / (serum creatinine (mg/dL) × 72). IBW is estimated by the following equations:

- Males: IBW (kg) = 50 kg + 2.3 kg for each inch over 5 feet
- Females: IBW (kg) = 45.5 kg + 2.3 kg for each inch over 5 feet

The summary of demographic data and baseline characteristics will be provided for the Safety Analysis Set.

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

A data listing of cirrhosis determination will be provided. A data listing will also be provided for subjects' prior HCV treatment and response.

5.2. Medical History

General medical history data will be collected at screening and listed only. General medical history data will not be coded.

6. EFFICACY ANALYSES

6.1. Primary Efficacy Endpoint

The primary efficacy endpoint is SVR 12 weeks after treatment discontinuation (SVR12) defined as HCV RNA < LLOQ (ie, < 15 IU/mL) 12 weeks after study drug cessation for the FAS. The COBAS® AmpliPrep/COBAS® TaqMan® HCV Test will be used to determine HCV RNA results in this study.

The 2-sided 95% exact confidence interval (CI) based on Clopper-Pearson method will be provided for the SVR12 rate.

6.2. Secondary Efficacy Endpoints

6.2.1. Definition of Secondary Efficacy Endpoints

Secondary efficacy endpoints include the following:

- The proportion of subjects who attain SVR at 4 and 24 weeks after treatment discontinuation, defined as HCV RNA < LLOQ (ie, < 15 IU/mL) 4 and 24 weeks after stopping treatment (SVR 4 and SVR 24)
- The proportion of subjects with HCV RNA below LLOQ (ie, < 15 IU/mL) by study visit
- HCV RNA (log_{10} IU/mL) and change from baseline in HCV RNA (log_{10} IU/mL) through end of treatment
- The proportion of subjects with virologic failure as the following:

  On-treatment virologic failure

  - HCV RNA ≥ LLOQ after having previously had 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 8 weeks of treatment (ie, nonresponse)

  Relapse

  - HCV RNA ≥ LLOQ during the posttreatment period having achieved HCV RNA < LLOQ at end of treatment, confirmed with 2 consecutive values or last available posttreatment measurement

6.2.2. Analysis Methods for Secondary Efficacy Endpoints

For analyses of HCV RNA < LLOQ (ie, < 15 IU/mL) 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 categorical imputation rules described in Section 3.6.1. The 2-sided 95% exact confidence interval based on Clopper-Pearson method will be provided for the proportion. 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.

Graphs for the proportion of subjects with HCV RNA < LLOQ over time during treatment will be displayed.

Summary statistics will be presented for absolute values and change from baseline in HCV RNA (log_{10} IU/mL) by visit through end of treatment (EOT). 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.

For the SVR12 endpoint analysis, a summary table of the number and percentage of subjects with SVR12, virologic failure (VF), 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 VF 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.

A concordance table between SVR12 and SVR24 will be provided. Subjects with both observed SVR12 and observed SVR24 data will be included for this analysis.

In addition, the proportion of subjects with ALT normalization (defined as ALT > ULN at baseline and ALT ≤ ULN at each visit) will be presented by study visit. Tables for ALT normalization by visit will use methodology similar to the analyses of HCV RNA < LLOQ, but will use a missing = excluded analysis. Only those subjects with ALT > ULN at baseline (defined as the last ALT value collected prior to first dose of study drug) will be included in the analysis of ALT normalization.

7. SAFETY ANALYSES

Safety data will be summarized for subjects included in the safety analysis set. Summaries of safety data (treatment-emergent [TE] adverse events [AEs], TE maximum toxicity grades, changes from baseline in laboratory tests and vital signs parameters) will include all data collected on or after the first dose date of study drug through the last dose date of study drug plus 30 days for subjects who have stopped the study drug.

All safety data (except for laboratory tests with results that were cancelled by the lab) will be included in data listings based on the Safety Analysis Set.

7.1. Adverse Events and Deaths

7.1.1. Adverse Event Dictionary

Clinical and laboratory 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 according to toxicity criteria specified in the protocol. The severity grade of events for which the investigator did not record severity will be categorized as “missing” for tabular summaries and data listings. The missing category will be listed last in summary presentation.

7.1.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected “Related” on the AE CRF to the question of “Related to Study Treatment.” Relatedness will always default to the investigator’s choice, not that of the medical monitor. Events for which the investigator did not record relationship to study drug will be considered related to study drug for summary purposes. However, by-subject data listings will show the relationship as missing.

7.1.4. Serious Adverse Events

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

7.1.5. Treatment-Emergent Adverse Events

7.1.5.1. Definition of Treatment-Emergent Adverse Events

Treatment-emergent AEs (TEAEs) are defined as 1 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 the AE is incomplete and the AE stop date is not prior to the first dosing date of study drug, then the month and year (or year alone if month is not recorded) of onset determine whether an AE is treatment emergent. The event is considered treatment emergent if both of the following 2 criteria are met:

- The AE onset is the same as or after the month and year (or year) of the first dosing date of study drug, and
- The AE onset date is the same as or before the month and year (or year) of the date corresponding to 30 days 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 dosing date of study drug, will be considered to be treatment emergent. In addition, an AE with the onset date missing and incomplete stop date with the same or later month and year (or year alone if month is not recorded) as the first dosing date of study drug will be considered treatment emergent.

7.1.6. Summaries of Adverse Events and Deaths

Treatment-emergent AEs will be summarized based on the Safety Analysis Set.

Summaries (number and percentage of subjects) of adverse events (by SOC and PT) will be provided using the safety analysis set as follows:

- All TE AEs
- Combined Grade 3 or 4 TE AEs
- Combined Grade 2, 3 or 4 TE AEs
- TE nonserious AEs occurring in at least 5% of subjects (this will be produced for ClinicalTrials.gov website)
- TE treatment-related AEs

- Combined Grade 3 or 4 TE treatment-related AEs
- Combined Grade 2, 3 or 4 TE treatment-related AEs
- TE SAEs
- TE treatment-related SAEs
- AEs leading to permanent discontinuation from the study drug
- AEs leading to interruption of the study drug

A brief, high-level summary of AEs described above will be provided by the number and percentage of subjects who experienced the above AEs. All deaths observed in the study will also be included in this summary.

Multiple events will be counted only once per subject in each summary. Adverse events will be summarized and listed first in alphabetic order of SOC and then by PT in descending order of total frequency within each SOC. For 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, all TEAEs and TE treatment-related AEs will be summarized by PT only, in descending order of total frequency.

Data listings, with a variable indicating whether the event is treatment-emergent, will be provided for the following:

- All AEs
- All AEs of Grade 3 or higher
- SAEs
- Deaths
- AEs leading to premature discontinuation of study drug

7.2. Laboratory Evaluations

Laboratory data collected during the study will be analyzed and 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 of study drug plus 30 days for subjects who have permanently discontinued study drug. The analysis will be based on values reported in conventional units. When values are below the LOQ, they will be listed as such, and the closest imputed value will be used for the purpose of calculating summary statistics as

specified in Section 3.7. Hemolized test results will not be included in the analysis, but they will be listed in by-subject laboratory listings.

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 coagulation and other laboratory tests. 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 formal statistical testing is planned.

7.2.1. Summaries of Numeric Laboratory Results

Descriptive statistics (n, mean, SD, median, Q1, Q3, minimum and maximum) will be provided for ALT, AST, total bilirubin, alkaline phosphatase, white blood cell (WBC) counts, neutrophils, lymphocytes, hemoglobin, platelets, reticulocytes, creatinine, INR, and creatinine clearance (calculated by the Cockcroft-Gault equation, using IBW) as follows:

- Baseline values
- Values at each postbaseline analysis window
- Change from baseline at each postbaseline analysis window

A baseline laboratory value will be defined as the last measurement obtained on or prior to the date/time 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 values will be displayed to the reported number of digits; SD values will be displayed to the reported number of digits plus 1.

In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.8.3.

The number of subjects with hemoglobin < 10 g/dL and < 8.5 g/dL at any postbaseline visits (up to 30 days after the last dose of any study drug) will be summarized.

7.2.2. Graded Laboratory Values

The Gilead Grading Scale for Severity of Adverse Events and Laboratory Abnormalities will be used for assignment of toxicity grades to laboratory results for purposes of analysis as Grade 0, Grade 1 (mild) , Grade 2 (moderate), Grade 3 (severe) or Grade 4 (potentially life threatening). Grade 0 includes all values that do not meet the criteria for an abnormality of at least Grade 1. For laboratory tests with 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, any abnormality of at least Grade 1 observed within the time frame specified above 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 by lab test; subjects will be categorized according to the most severe postbaseline abnormality grade for a given lab test:

- TE Graded laboratory abnormalities
- TE Grade 3 or 4 laboratory abnormalities

For all summaries of laboratory abnormalities, the denominator is the number of subjects with nonmissing postbaseline values up to 30 after last dosing date.

A by-subject listing of treatment-emergent Grade 3 or 4 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 lab test of interest, with all applicable severity grades displayed.

All valid laboratory values will be listed. Values falling outside of the relevant reference range and/or meeting Gilead Grading Scale will be flagged, as appropriate, in the data listings.

7.3. 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 study drug

Use of concomitant medications will be summarized by Anatomical Therapeutic Chemical (ATC) drug class Level 2 and preferred name using the number and percentage of subjects. 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 will be ordered alphabetically by ATC medical class and then by preferred term in descending overall frequency within each ATC medical class. For drugs with the same frequency, sorting will be done alphabetically.

For purposes of programming, any medication with a stop date that is on/prior to first dosing date or start date that is after the last dose of any study drug will be excluded from this summary. Otherwise, dates that are completely missing will be included in the summary. If a partial stop date is entered, then the month and year (if day is missing) or year (if day and month are missing) that is prior to the study drug start date will be excluded from the summary. If a partial start date is entered, then the month and year (if day is missing) or year (if day and month are missing) that is after the study drug stop date will be excluded from the summary. Medications with completely missing start and stop dates will be included in the concomitant medication summary, unless otherwise specified. Summaries will be based on the Safety Analysis Set. No formal statistical testing is planned.

A summary of concomitant medications will be provided.

All prior and concomitant medications (other than per-protocol study drugs) will be provided in a by-subject listing sorted by subject ID number and administration date in chronological order.

7.4. Body Weight, Height, BMI and Vital Signs

Absolute value and change from baseline in vital signs (systolic blood pressure [SBP], diastolic blood pressure [DBP] and pulse) at each visit will be summarized for the Safety Analysis Set using descriptive statistics by treatment cohort for each postbaseline analysis window. In the case of multiple values in an analysis window, data will be selected for analysis as described in Section 3.8.3. No inferential statistics will be generated.

A listing of height (at screening), body weight, and BMI, and a listing of SBP, DBP, pulse, respiration and temperature will be provided.

7.5. Electrocardiogram (ECG) Results

Absolute value and change from baseline in PR interval, QRS interval, QT interval and QTcF at each visit will be summarized for the Safety Analysis Set using descriptive statistics by treatment cohort for each postbaseline analysis window. A listing of PR interval, QRS interval, QT interval, and QTcF will be provided.

A listing of overall assessment of ECG results including description regarding clinically significant abnormalities will be provided.

7.6. Echocardiogram Results

Absolute value and change from baseline in ejection fraction, fractional shortening, left ventricular end diastolic volume (LVEDV) and left ventricular internal dimension in diastole (LVIDd) at each visit will be summarized for the safety analysis set using descriptive statistics by treatment cohort for each postbaseline visit. A shift table of diastolic function score assessment at baseline versus each on-treatment visit will be presented.

A listing of ejection fraction, fractional shortening, LVEDV, LVIDd and diastolic function score will be provided.

7.7. Other Safety Measures

A data listing will be provided for subjects who received dialysis during the study.

A data listing will be provided for subjects who become pregnant during the study.

7.8. Changes From Protocol-Specified Safety Analyses

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

8. PHARMACOKINETIC (PK) ANALYSES

Steady-state PK over the dosing interval will be determined from intensive PK assessments at the Week 2 or Week 4 on-treatment visit.

Concentration of SOF (and its metabolites GS-566500 and GS-331007) and LDV in plasma will be determined using validated bioanalytical assays. The PK parameters for these analytes will be computed for all subjects with evaluable PK profiles. For each subject, the following PK parameters will be calculated, as appropriate:

Parameter	Description
AUC_{tau}	area under the concentration versus time curve over the dosing interval
C_{last}	last observed quantifiable concentration of the drug in plasma
C_{max}	maximum observed concentration of drug in plasma
C_{tau}	observed drug concentration at the end of the dosing interval
$t_{1/2}$	estimate of the terminal elimination half-life of the drug in plasma, calculated by dividing the natural log of 2 by the terminal elimination rate constant (λ_z)
T_{last}	time (observed time point) of C_{last}
T_{max}	time (observed time point) of C_{max}
λ_z	terminal elimination rate constant, estimated by linear regression of the terminal elimination phase of the plasma concentration of drug versus time curve

PK parameters will be estimated by application of a nonlinear model using standard noncompartmental methods (WinNonlin® software). The linear up/log down trapezoidal rule will be used in conjunction with the appropriate noncompartmental model (usually input Model 200 for oral dosing), with input values for dose, time of dose, plasma concentration, and corresponding real time values, based on drug dosing times whenever possible. In oder to calculate AUCtau (dosing interval = 24 h), the pre-dose concentration will also be used as the 24h concentration since these samples are obtained at steady state conditions. However, missing concentrations from scheduled PK time-points will not be imputed.

All predose sample times of less than time zero will be converted to zero. Samples below the limit of quantitation of the bioanalytical assays that occur prior to the achievement of the first quantifiable concentration will be assigned a concentration value of zero to prevent overestimation of the initial AUC. Samples that are BLQ at all other time points will be treated as missing data. The nominal time point for a key event or dosing interval (tau) may be used to permit direct calculation of AUC over specific time intervals. The appropriateness of this approach will be assessed by the pharmacokineticist on a profile-by-profile basis.

Accurate estimation of several PK parameters, such as λ_z and $t_{1/2}$, are dependent on the measured terminal elimination phase of the drug. The appropriateness of calculating these parameters will be assessed by the pharmacokineticist on a profile-by-profile basis.

Ten descriptive statistics (sample size, mean, SD, coefficient of variation [%CV], median, Q1, Q3, minimum, maximum, and geometric mean and its 95% CI) will be presented for PK concentration data and PK parameter data. For concentration values BLQ, the number of subjects with values of BLQ will be presented.

Plasma concentrations of SOF (and its metabolites GS-566500 and GS-331007) and LDV over time from the intensive PK assessments will be plotted in linear and semi-logarithmic scales as mean ± SD and as Q1, median, and Q3 by visit.

9. SOFTWARE

SAS® Software Version 9.4. SAS Institute Inc., Cary, NC, USA.

Phoenix® WinNonlin®, Version 6.4, Pharsight Corporation, Mountain View, CA, USA.

10. SAP REVISION

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

11. APPENDICES

Appendix 1. Schedule of Assesments for Cohort 3

Study Procedure	Screen[a]	Day 1[b]	Treatment Visits[i]							Post-Treatment Visits[j]			ET[c]
			Week 1	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12	Week 4	Week 12	Week 24	
Written Informed Consent	X												
Medical History	X												
HCV RNA Genotype	X												
IL28B Genotyping	X												
HbA1c	X												
HCV, HBV, HIV Serology	X												
TSH	X												
Physical Exam, including Vital Signs[d]	X	X	X	X	X	X	X	X	X	X	X	X	X
12-lead ECG	X	X			X		X		X	X	X	X	X
Echocardiogram	X								X				
Height	X												
Weight	X												
Hematology	X	X	X	X	X	X	X	X	X	X	X	X	X
Coagulation (PT, PTT, and INR)	X	X				X				X			X
Chemistry	X	X	X	X	X	X	X	X	X	X	X	X	X
HCV RNA Viral Load	X	X	X	X	X	X	X	X	X	X	X	X	X
HCV RNA Sequencing		X	X	X	X	X	X	X	X	X	X	X	X

Study Procedure	Screen[a]	Day 1[b]	Treatment Visits[i]							Post-Treatment Visits[j]			ET[c]
			Week 1	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12	Week 4	Week 12	Week 24	
Serum Pregnancy Test[e]	X	X			X		X		X	X	X	X	X
Creatinine Clearance	X												
Optional Pharmacogenetic Sample[k]		X											
Intensive PK				X[f]	X[f]								
Trough PK Sample[g]			X			X	X	X	X				X
Archive Plasma Sample		X	X	X	X	X	X	X	X	X	X	X	X
Study Drug Administration		X	Weeks 1-12										
Review Dosing Diary/ Perform Accountability[h]			X	X	X	X	X	X	X				
AEs/Concomitant Meds	X	X	X	X	X	X	X	X	X	X	X	X	X

a Screening evaluations must be completed within 42 days prior to Day 1.

b Day 1 tests and procedures must be completed prior to administration of the first dose of study drugs

c Within 72 hours of permanently discontinuing study drug.

d Full PE at Day 1 and ET visits only; symptom-directed PE at all other timepoints. Vital signs include blood pressure, pulse, respiration rate, and temperature

e Females of childbearing potential only. To confirm eligibility at Day 1, a urine pregnancy test may be collected for subjects able to pass urine. For subjects unable to pass urine, a serum pregnancy test at Day 1 must be performed at a local lab prior to dosing to confirm eligibility along with sample collected and send to central lab. During post-treatment of the study, serum or urine pregnancy testing will occur every month during non-clinic post treatment visits. The subject will be contacted by telephone to confirm that pregnancy testing has been performed post-treatment during non-clinic visits.

f Intensive plasma PK evaluations will be assessed at the following timepoints: 0 (predose -5 minutes), 0.25, 0.5, 1, 2, 4, 6, 8, 10, and 12 hours postdose once either on Week 2 **OR** 4, per investigator discretion.

g Trough plasma PK samples will be drawn prior to dosing.

h Dosing Diaries will be completed for all non-observed doses and will be reviewed at every visit. Unused study drug will be returned to perform study drug accountability in the original container at each visit following Day 1 for study drug compliance assessment.

i A window of ± 2 days is allowed for the treatment visits on weeks 1, 2, and 12. A window of ± 4 days is allowed for the treatment visits weeks, and 4-10. Subjects who cannot complete their study visit per the visit schedule should ensure they do not run out of study drug prior to their next study visit. Compliance is critical to ensure adequate drug exposure.

j A window of ± 7 days is allowed for the post treatment visits.

k The sample should be collected on Day 1 prior to dosing, but may be collected at any time during the study or at a separate post-study visit, if necessary.

Appendix 2. Tables, Figures, and Listings

Table Number	Title	Analysis Set
15.8.1.1	Subjects Enrolled and Treated by Country and Investigator	Safety Analysis Set
15.8.1.2	Subject Disposition	Screened Subjects
15.8.1.3	Reasons for Screen Failure	Screened Subjects
15.8.3	Demographics and Baseline Characteristics	Safety Analysis Set
15.8.4	Adherence to Study Drug	Safety Analysis Set
15.9.1	SVR12	Full Analysis Set
15.9.2.1	Virologic Outcomes	Full Analysis Set
15.9.2.2	SVR by Visit During Posttreatment Follow Up	Full Analysis Set
15.9.2.3	Concordance between SVR12 and SVR24	Full Analysis Set
15.9.2.4	Proportion of Subjects with HCV RNA Less than LLOQ (15 IU/mL) While on Treatment by Visit	Full Analysis Set
15.9.2.5	HCV RNA (log10 IU/mL) and Change from Baseline by Visit Through End of Treatment	Full Analysis Set
15.9.2.6	Proportion of Subjects with ALT Normalization by Visit	Full Analysis Set with ALT>ULN at Baseline
15.10.1.1.1	Individual Data and Summary Statistics of Plasma Intensive Concentration (ng/mL) at Protocol-Specified Sampling Times by Visit	SOF PK Analysis Set
15.10.1.1.2	Individual Data and Summary Statistics of Plasma Intensive Concentration (ng/mL) at Protocol-Specified Sampling Times by Visit	GS-566500 PK Analysis Set
15.10.1.1.3	Individual Data and Summary Statistics of Plasma Intensive Concentration (ng/mL) at Protocol-Specified Sampling Times by Visit	GS-331007 PK Analysis Set
15.10.1.1.4	Individual Data and Summary Statistics of Plasma Intensive Concentration (ng/mL) at Protocol-Specified Sampling Times by Visit	LDV PK Analysis Set
15.10.1.2.1	Individual Estimate and Summary Statistics for Pharmacokinetic Parameters by Visit	SOF PK Analysis Set
15.10.1.2.2	Individual Estimate and Summary Statistics for Pharmacokinetic Parameters by Visit	GS-566500 PK Analysis Set
15.10.1.2.3	Individual Estimate and Summary Statistics for Pharmacokinetic Parameters by Visit	GS-331007 PK Analysis Set
15.10.1.2.4	Individual Estimate and Summary Statistics for Pharmacokinetic Parameters by Visit	LDV PK Analysis Set
15.11.1	Duration of Exposure to Study Regimen	Safety Analysis Set
15.11.2.1.1	Adverse Events: Brief Summary	Safety Analysis Set
15.11.2.1.2	All Treatment-Emergent Adverse Events	Safety Analysis Set
15.11.2.1.3	All Treatment-Emergent Adverse Events by Preferred Term	Safety Analysis Set

Table Number	Title	Analysis Set
15.11.2.1.4	Treatment-Emergent Non-Serious AEs Occurring in At Least 5% of Subjects	Safety Analysis Set
15.11.2.2.1	Grade 3 or 4 Treatment-Emergent Adverse Events	Safety Analysis Set
15.11.2.2.2	Grade 2, 3, or 4 Treatment-Emergent Adverse Events	Safety Analysis Set
15.11.2.3.1	Treatment-Emergent Treatment-Related Adverse Events	Safety Analysis Set
15.11.2.3.2	Treatment-Emergent Treatment-Related Adverse Events by Preferred Term	Safety Analysis Set
15.11.2.3.3	Grade 3 or 4 Treatment-Emergent Treatment-Related Adverse Events	Safety Analysis Set
15.11.2.3.4	Grade 2, 3, or 4 Treatment-Emergent Treatment-Related Adverse Events	Safety Analysis Set
15.11.4.1	Treatment-Emergent Serious Adverse Events	Safety Analysis Set
15.11.4.3	Treatment-Emergent Treatment-Related Serious Adverse Events	Safety Analysis Set
15.11.5.1	Adverse Events Leading to Premature Discontinuation of Study Drug	Safety Analysis Set
15.11.5.2	Adverse Events Leading or Interruption of Study Drug	Safety Analysis Set
15.11.6.1.1	Hemoglobin (g/dL) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.1.2	Subjects with Postbaseline Hemoglobin < 10 g/dL and < 8.5 g/dL	Safety Analysis Set
15.11.6.1.3	Reticulocytes (x10^3 /uL) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.1.4	WBC (x10^3 /uL) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.1.5	Neutrophils (x10^3 /uL) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.1.6	Lymphocytes (x10^3 /uL) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.1.7	Platelets (x10^3 /uL) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.2.1	ALT (U/L) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.2.2	AST (U/L) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.2.3	Total Bilirubin (mg/dL) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.2.4	Alkaline Phosphatase (U/L) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.2.5	Creatinine (mg/dL) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.2.6	Estimated Glomerular Filtration Rate by Cockcroft-Gault (mL/min) and Change from Baseline by Visit	Safety Analysis Set
15.11.6.3	INR and Change from Baseline by Visit	Safety Analysis Set
15.11.6.4.1	Treatment-Emergent Graded Laboratory Abnormalities	Safety Analysis Set
15.11.6.4.2	Treatment-Emergent Grade 3 or 4 Laboratory Abnormalities	Safety Analysis Set
15.11.7.1.1	Systolic Blood Pressure (mmHg) and Change from Baseline by Visit	Safety Analysis Set
15.11.7.1.2	Diastolic Blood Pressure (mmHg) and Change from Baseline by Visit	Safety Analysis Set
15.11.7.1.3	Pulse (bpm) and Change from Baseline by Visit	Safety Analysis Set
15.11.7.3	Concomitant Medications	Safety Analysis Set

Table Number	Title	Analysis Set
15.11.9.1	Summary of On-Treatment ECG Abnormality	Safety Analysis Set
15.11.9.2.1	PR Interval (ms) and Change from Baseline by Visit	Safety Analysis Set
15.11.9.2.2	QRS Interval (ms) and Change from Baseline by Visit	Safety Analysis Set
15.11.9.2.3	QT Interval (ms) and Change from Baseline by Visit	Safety Analysis Set
15.11.9.2.4	QTcF (ms) and Change from Baseline by Visit	Safety Analysis Set
15.11.10.1.1	Echocardiogram: Ejection Fraction (%) and Change from Baseline by Visit	Safety Analysis Set
15.11.10.1.2	Echocardiogram: Fractional Shortening (%) and Change from Baseline by Visit	Safety Analysis Set
15.11.10.2.1	Echocardiogram: LVEDV (mL) and Change from Baseline by Visit	Safety Analysis Set
15.11.10.2.2	Echocardiogram: LVIDd (cm) and Change from Baseline by Visit	Safety Analysis Set
15.11.10.3	Echocardiogram: Shift Table of Baseline versus On-Treatment Diastolic Function Score Assessment by Visit	Safety Analysis Set

Figure Number	Title	Analysis Set
15.8.1	Subject Disposition	Screened Subjects
15.9.2.3	Proportion of Subjects with SVR (HCV RNA < LLOQ) by Posttreatment Visit	Full Analysis Set
15.9.2.4	Proportion of Subjects with HCV RNA < LLOQ While on Treatment by Visit	Full Analysis Set
15.10.1.1.1	Mean (SD) Plasma Concentration - Time (0 hour - 12 hours) Profiles by Visit	SOF PK Analysis Set
15.10.1.1.2	Mean (SD) Plasma Concentration - Time (0 hour - 12 hours) Profiles by Visit	GS-566500 PK Analysis Set
15.10.1.1.3	Mean (SD) Plasma Concentration - Time (0 hour - 12 hours) Profiles by Visit	GS-331007 PK Analysis Set
15.10.1.1.4	Mean (SD) Plasma Concentration - Time (0 hour - 12 hours) Profiles by Visit	LDV PK Analysis Set
15.10.1.1.5	Median (Q1, Q3) Plasma Concentration - Time (0 hour - 12 hours) Profiles by Visit	SOF PK Analysis Set
15.10.1.1.6	Median (Q1, Q3) Plasma Concentration - Time (0 hour - 12 hours) Profiles by Visit	GS-566500 PK Analysis Set
15.10.1.1.7	Median (Q1, Q3) Plasma Concentration - Time (0 hour - 12 hours) Profiles by Visit	GS-331007 PK Analysis Set
15.10.1.1.8	Median (Q1, Q3) Plasma Concentration - Time (0 hour - 12 hours) Profiles by Visit	LDV PK Analysis Set

Listing Number	Title	Analysis Set
16.1.6	Lot Number and Kit ID	Safety Analysis Set
16.2.1.3	Subject Disposition	Safety Analysis Set
16.2.1.4	Reasons for Screen Failure	Subjects Screened But Not Enrolled
16.2.2.1	Eligibility Criteria Deviations	Safety Analysis Set
16.2.4.1	Subject Demographics and Baseline Characteristics	Safety Analysis Set
16.2.4.2	Cirrhosis Determination	Safety Analysis Set
16.2.4.3.1	Medical History	Safety Analysis Set
16.2.4.3.2	Prior HCV Treatment and Response	Safety Analysis Set
16.2.4.4	Prior and Concomitant Medications	Safety Analysis Set
16.2.5.1	Study Drug Administration	Safety Analysis Set
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
16.2.6.1	HCV RNA (log10 IU/mL) and Change from Baseline	Safety Analysis Set
16.2.6.2	Subjects with Virologic Failure	Safety Analysis Set
16.2.6.3	Subjects with 'Other' Virologic Outcome	Safety Analysis Set
16.2.6.4	Subjects with Relapse After Posttreatment Week 12	Safety Analysis Set
16.2.7.1	All Adverse Events	Safety Analysis Set
16.2.7.2.1	Deaths	Safety Analysis Set
16.2.7.3	Serious Adverse Events	Safety Analysis Set
16.2.7.4	Grade 3 or 4 Adverse Events	Safety Analysis Set
16.2.7.5	Adverse Events Leading to Premature Discontinuation from Any Study Drug	Safety Analysis Set
16.2.8.1.1	Subjects with Postbaseline Hemoglobin < 10 g/dL and <8.5 g/dL	Safety Analysis Set
16.2.8.1.2	Central Laboratory (Covance) Reference Ranges	Safety Analysis Set
16.2.8.1.3	Subjects with Treatment-Emergent Grade 3 or 4 Laboratory Abnormalities	Safety Analysis Set
16.2.8.1.4	Screen Labs: HBsAg, Anti-HIV Ab, Anti-HCV Ab, HbA1c, and Serum Beta hCG	Safety Analysis Set
16.2.8.1.5.1	Hematology: Hematocrit, Hemoglobin, Reticulocyte Count, 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

Listing Number	Title	Analysis Set
16.2.8.1.6.1	Chemistry: Sodium, Potassium, Serum Creatinine, Estimated GFR (Cockcroft-Gault), and Glucose	Safety Analysis Set
16.2.8.1.6.2	Chemistry: AST, ALT, Total Bilirubin, Direct Bilirubin, Alkaline Phosphatase, GGT, and Albumin	Safety Analysis Set
16.2.8.1.7	Coagulation and Other Laboratory Tests: INR, APTT, and TSH	Safety Analysis Set
16.2.8.2.1	Vital Signs	Safety Analysis Set
16.2.8.2.2	Height, Weight, and BMI	Safety Analysis Set
16.2.8.2.3.1	Overall Assessment of Electrocardiogram Results	Safety Analysis Set
16.2.8.2.3.2	Electrocardiogram measurements	Safety Analysis Set
16.2.8.3.1	Echocardiogram Results	Safety Analysis Set
16.2.8.3.2	Echocardiogram: Ejection Fraction and LVEDV	Safety Analysis Set
16.2.8.4	Dialysis	Safety Analysis Set
16.2.8.5	Pregnancy	Safety Analysis Set
16.2.8.6	Comments	Safety Analysis Set