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Protocol Title:	Real world evidence study of the effectiveness of Paritaprevir/r – Ombitasvir + Dasabuvir without Ribavirin in patients with chronic HCV Gt1b infection and compensated liver cirrhosis in the Russian Federation – an observational, multi-center study
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REVISION HISTORY

№	Version	Date	Changes
1	1.0	16.08.2017	New Document
2	2.0	16.03.2018	1) section 9 and corresponding tables shells was updated. – additionally to efficiency endpoints the following virologic outcomes were added to the analysis: breakthrough, failure to suppress and premature study drug discontinuation with no on-treatment virologic failure; – due to the fact that in the Russian clinical practice tests for HCV RNA often have limit of detection higher than 50 IU/mL and may vary across laboratories, the definitions for effectiveness outcomes were adjusted; – additional frequency tables for patients in subgroup without missing SVR12 data category were added; – method of 95% confidence interval calculation for odds ratio in logistic regression analysis was specified; 2) the information about time windows for clinical laboratory data was moved to section 4.1 "General study design and plan"; 3) tables shells for demographics and baseline characteristics was changed: one table was divided into several tables; 4) list of tables, figures and listings was added.

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1 Abbreviations and definitions

The abbreviations and the definitions used in this document are listed below.

Abbreviation	Abbreviation in Full
ABBVIE REGIMEN	Paritaprevir/r – Ombitasvir ± Dasabuvir
AE	Adverse event
ATC	Anatomical therapeutic chemical code
BL	Baseline
BMI	Body mass index
CHC	Chronic hepatitis C
CI	Confidence interval
CRF	Case report form
CSR	Clinical study report
DMC	Data monitoring Committee
eCRF	Electronic CRF
EoT	End of treatment
ICH	International conference on Harmonisation
IL28B	Interleukin 28B
INR	International normalized ratio
IQR	Interquartile range
LLoD	Limit of detection
LLoQ	Lower limit of quantification
PT	Preferred term
RBV	Ribavirin
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SOC	System organ class
SOP	Standard operational procedure
SVR	Sustained virological response
SVR12	SVR at 12 weeks after EoT
ULoQ	Upper limit of quantification
WHO	World Health Organization
WHODD	WHO drug dictionary

2 Introduction

This document describes the planned data statistical analysis of an observational, multicenter, real world evidence study of the effectiveness of Paritaprevir/r – Ombitasvir + Dasabuvir without Ribavirin in patients with chronic HCV Gt1b infection and compensated liver cirrhosis in the Russian Federation (CITRIN).

This SAP is written according to ICH E9 Guideline [1] and Data MATRIX LLC SOP [2] using the Protocol Final version 1.0 dated 29 Nov 2016 and CRF Final version 1.1 dated 16 Mar 2017.

The purpose of this document is to provide a more technical and detailed elaboration of the principal features of the analysis, described in the Protocol, and to include detailed procedures for executing the statistical analysis.

The SAP needs to be finalized and signed prior to database soft lock. Revisions to the approved SAP may be made prior to database soft lock. In case of deviation from the finalized SAP, explanation will be provided in the clinical study report (CSR).

3 Study objectives and variables[1]

3.1 Study objectives

The research question of this study is what is the effectiveness of the interferon-free 3DAA ABBVIE REGIMEN without RBV in patients with HCV Gt1b infection and compensated liver cirrhosis in a real life setting?

The Protocol defines the following *primary objective* of this study:

- to describe the effectiveness of the interferon-free 3DAA ABBVIE REGIMEN without RBV in patients with HCV Gt1b infection and compensated liver cirrhosis as evidenced by sustained virological response at 12 weeks after the end of treatment in routine clinical practice.

The Protocol defines the following *secondary objectives* of this study:

- to describe the EoT response rate;
- to assess the rate of relapse (timeframe for assessing relapse - between EoT and SVR 12);
- to describe baseline characteristics of patients with HCV Gt1b and compensated cirrhosis treated with AbbVie 3D regimen;
- to collect information on co-morbidities and concomitant medications in cirrhotic patients in the Russian population;
- to describe the tolerability of the ABBVIE REGIMEN.

[1] This section is based on the sections 8 “Research Question and Objectives”, 9.9 “Variables”, 9.13.4 “Primary Effectiveness Endpoints” and 9.13.5 “Secondary Effectiveness Endpoints” of clinical study Protocol.

3.2 Variables

The primary variable of this study (and also effectiveness endpoint) is:
- the percentage of patients achieving SVR12 (single last HCV RNA <50 IU/mL 12 weeks [i.e. at least 84 days] after the last actual dose of the ABBVIE REGIMEN) is the primary effectiveness endpoint.

The secondary variables of this study are:
- effectiveness endpoints:
  - the percentage of patients with virological response (HCV RNA <50 IU/mL) at EoT;
  - the percentage of patients with relapse after EoT (defined as HCV RNA <50 IU/mL at EoT followed by HCV RNA ≥50 IU/mL);
  - the percentage of patients with relapse during treatment phase[1] (defined as at least one documented HCV RNA <50 IU/mL followed by HCV RNA ≥50 IU/mL during treatment);
  - the number and percentage of patients meeting each and any of the following SVR12 non-response categories:
    - relapse during post-treatment phase (defined as HCV RNA <50 IU/mL at EoT or at the last on-treatment HCV RNA measurement followed by HCV RNA ≥50 IU/mL post-treatment);
    - missing SVR12 data and/or none of the above criteria;
- descriptive statistics for baseline characterictics;
- the number and percentage of patients with comorbidities and concomitant medications.
- the number and percentage of patients with adverse events.

4 Study design

4.1 General study design and plan[2]

This is a post-marketing, prospective, multicenter, observational study in patients receiving the interferon-free ABBVIE REGIMEN (Paritaprevir/r – Ombitasvir ± Dasabuvir) without RBV.

This study is focusing on collecting real-world data. Adult patients chronically infected with HCV and compensated liver cirrhosis, receiving the interferon-free ABBVIE REGIMEN will be offered to participate in this study during a routine clinical visit at the participating sites. The prescription of a treatment regimen is at the discretion of the physician in accordance with local clinical practice and label, is made independently from this observational study and precedes the decision to offer a patient the opportunity to participate in this study.

After written Authorization (Consent) for Use/Disclosure of Data form (hereinafter – written patient authorization form) has been obtained, patient data including demographic data, HCV disease characteristics, co-morbidities, co-medication, treatment details, and laboratory assessments as recorded in the patient's medical records (source documentation) will be documented in the eCRF. Information for patients enrolled within 2 weeks after initiation of ABBVIE REGIMEN is collected at routine patient visits therefore baseline patient data should be taken from medical records. No patient identifiable information will be captured, a unique

[1] The EoT time point is included in the analyzed interval.
[2] This section is based on the sections 9.1 "Study Design" and 9.8 "Description of Activities" of clinical study Protocol.

patient number will be automatically allocated by the web based eCRF system once the investigator or designee creates a new patient file.

Follow-up visits, treatment, procedures and diagnostic methods will follow physicians' routine clinical practice.

In the study, patients will be observed for the duration of the ABBVIE REGIMEN therapy and for up to 12 weeks after treatment completion. 12-week routine treatment regimen will include at least two observational visits (Visit 1 and EoT) plus one 30 days safety follow-up visit and one 12 weeks follow-up visit (SVR12) after the last dose of ABBVIE REGIMEN. 30 days safety follow-up visit can be done as telephone call contact. Additional observational visits between Visit 1 and EoT can be done in case of clinical necessity and physician decision.

In total, there will be at least four study visits. Patients who prematurely discontinue the study should return to the site to document EoT data.

The schedule of the study procedures is presented in table 4.1.

Table 4.1 – Program activities

Assessment/ Procedure *(only available data to be collected; no diagnostic or monitoring procedures to be applied to the patients apart from those of routine clinical practice)*	**Visit 1**	**Treatment period**	**Post-treatment period**	
		EoT (on-treatment visits)	**Safety Follow-up visit**	**SVR12 Follow-up visit**
Written patient authorization form	X			
Inclusion/Exclusion Criteria	X			
Demographic information	X			
IL28B	X			
Relevant CHC disease characteristics	X			
Liver fibrosis stage	X			
CHC treatment history	X			
HCV genotype and subtype	X			
HCV RNA samples	X	X		X
Clinical chemistry and hematology	X	X		X
ABBVIE REGIMEN initiation documentation	X			
ABBVIE REGIMEN adherence	X	X		
Concomitant medication	X	X		X
Relevant medical history, co-morbidities	X			
SAE, non-serious AE and pregnancy reporting	X	X	X	X

Time windows for reported clinical laboratory test results are described in the table 4.2.

Table 4.2 – Analysis time windows

Time point	**Time Window**
Visit 1	Last value prior to start of study treatment (i.e. ≤study day 1)
EoT[1]	Study day of last dose (from study day 56 to study day 98)
SVR12	last value between 57 and 112 days post the study day of last dose

[1] The EoT time window will not be used for t*he target population* analyses, actual collected EoT visit will be presented in this case even if EoT ≤study day 55 (less than 8 weeks).

4.1 Sample size[1]

60 patients will be included in this descriptive study without any prior sample size calculation.

4.2 Randomization and blinding

This study is observational with one treatment group. Randomization and blinding procedures are not applicable.

4.3 Planned analyses

The only final statistical analysis report will be performed for this study.
No analyses for DMC meetings and no interim analysis are planned in the study.

5 General considerations

Study Day will be calculated from the reference start date, and will be used to show start/ stop day of assessments and events.

Reference start date is defined as the day of the start treatment ("EXSTDTC" variable from "EX" domain of the database).

If the date of the event is on or after the reference date then
study day = (date of event – reference date) + 1.

If the date of the event is prior to the reference date then
study day = (date of event – reference date) – 1.

Baseline is defined as the measurement taken on Visit 1.

6 Analysis populations

The target population (TP) – all patients with signed written Patient Authorization, who fulfill the eligibility criteria. Patients who prematurely discontinue earlier than ≤study day 55 will be used in analyses on the target population with actual EoT time point without windowing conventions adjustment for EoT.

The core population (CP) – all patients of the TP, who have started and received the treatment combination recommended in the current local label for their disease characteristics. Patients with EoT ≤ study day 55 (less than 8 weeks) will be excluded from the CP (these patients will be included to the NCP).

The safety population (SP) – all patients who received at least one dose of the ABBVIE REGIMEN.

The non-core population (NCP) – patients not receiving the treatment recommended in the local label.

The core population with sufficient follow-up data (CPSFU) – all CP patients, who fulfil one of the following criteria:

– evaluable HCV RNA data within the SVR12 time window;

[1] This section is based on the section 9.11 "Study Size" of clinical study Protocol.

- a HCV RNA value ≥50 IU/mL at the last measurement post-baseline (i.e. no virological response achieved at the last measurement on-treatment or post-treatment);
- HCV RNA <50 IU/mL at the last measurement post-baseline, but no HCV RNA measurement on the SVR12 visit due to reasons related to safety (e.g. dropped out due to AE) or incomplete efficacy information (e.g. virologic failure such as relapse is reported in the eCRF but date and value of the corresponding HCV RNA test is missing).

In this way, only patients who had virological response at their last on-treatment or post-treatment measurement, but had no HCV RNA measurements within the SVR12 time window for reasons not related to safety or effectiveness (e.g. lost-to-follow-up or patient not willing to perform an additional HCV RNA test on the SVR12 visit) will be excluded from this analysis.

Figure 6.1 illustrates the rule of patient's allocation in the core population with sufficient follow-up data (CPSFU).

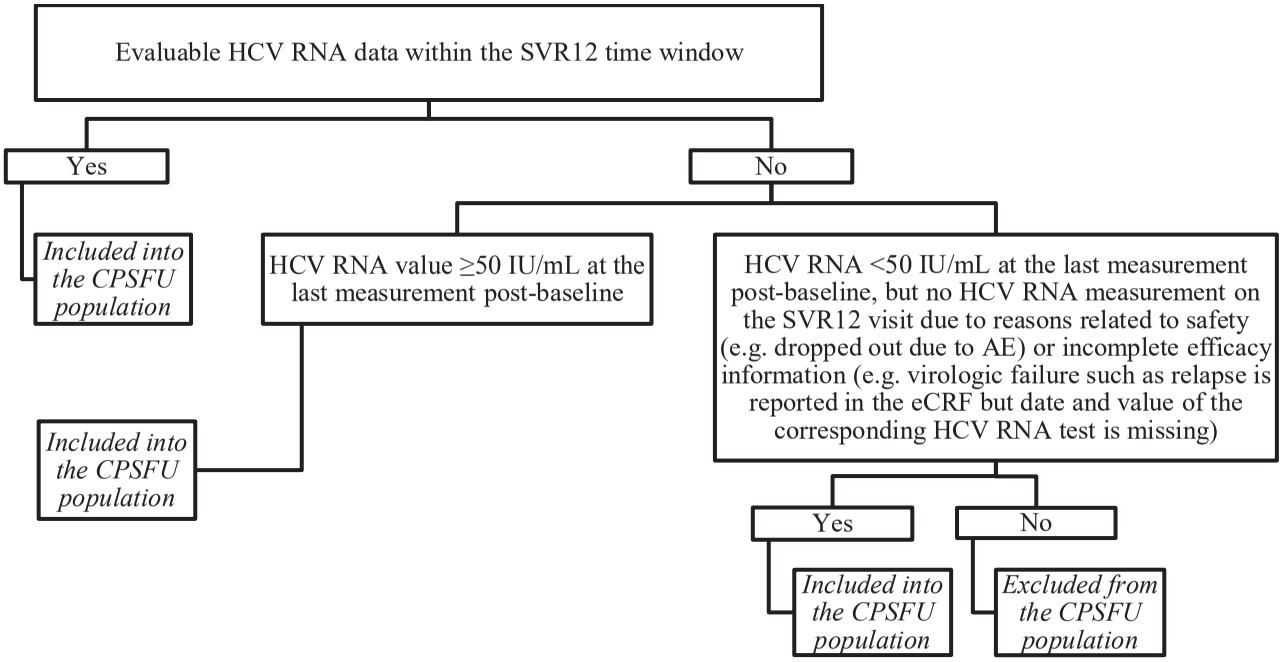

Figure 6.1 – The core population with sufficient follow-up data (CPSFU) allocation

7 Statistical considerations

7.1 Standard descriptive statistics

The data of continuous type will be presented with following statistics: *n* (the number of subjects with no missing data), mean, median, standard deviation (SD), interquartile range (IQR), minimum and maximum values. In quantitative tests the values less than LLoQ will be replaced to 1/2 of LLoQ, the values more than ULoQ will be replaced to ULoQ.

The data of categorical type (including clinical evaluations) will be presented with *n* (the number of subjects with no missing data), frequencies and percentages. Unless otherwise specified, percentages by categories will be based on the number of subjects with no missing data.

The number of decimals for each descriptive statistical value will be determined by the following rules:

- mean, median and IQR: +1 decimal symbol compared to the analyzed variable values;
- standard deviation: +2 decimal symbols compared to the analyzed variable values;
- minimum and maximum values: the same as for the analyzed variable values;
- percentages will be rounded to one decimal symbol;
- confidence intervals will be presented with accuracy of the estimated value.

7.2 Statistical tests and common calculations

The following arrangements will be applied:

- all tests will be two-sided with the default significant level 5%;
- confidence intervals will be 95% and will be determined using the Clopper-Pearson method;
- type I error values (p-values) will be rounded to four decimal symbols.

For quantitative measurements of clinical laboratory data, changes from baseline will be calculated as (measurement at visit X – measurement at baseline).

7.3 Missing data

If the information about adverse event start date and time is missing or incomplete, the following rules will be used for the classification of AEs for AEs of the study period and AEs, which occurred before the start of treatment:

Table 7.1 – AEs missing management.

Day	Month	Year	Processing
is missing	is known	is known	AE will be classified as AE of the study period, if month and year ≥ month and year of the first study drug administration date
is missing	is missing	is known	AE will be classified as AE of the study period, if year ≥ year of the first study drug administration date
is known	is missing	is known	
is missing	is known	is missing	AE will be classified as AE of the study period
is known	is missing	is missing	
is missing	is missing	is missing	

7.4 Multicenter studies

The study will take place in 5-7 centers (national and regional hospitals/outpatient services). Data from all centers will be merged and analyzed as one population for all study endpoints.

7.5 Multiple comparisons

No adjustments for multiplicity are required.

8 Summary of study data

Each study variable will be analyzed for relevant population.

Unless otherwise specified all raw data will be listed and sorted by unique subject identifier and study period/assessment (i.e. time point), where applicable.

Demographic and baseline characteristics, concurrent illnesses and medical conditions, prior and concurrent medications will be reported for *the core population* (*CP*).

The results will be presented overall and for the CP analysis groups based on genotype 1 subtype, fibrosis status and treatment experienced or naīve.

According to the eligibility criteria of this study[1], only patients with genotype 1b and Child Pugh A cirrhosis will be included in this study. In this way, the results will be presented for the CP analysis groups by the following parameters:

- cirrhosis score[2] (5 or 6);
- treatment experienced or naīve patients[3] (with/without prior treatment for CHC).

Additionally demographic and baseline characteristics, concurrent illnesses and medical conditions, prior and concurrent medications will be reported for *the target population* (*TP*) and *the safety population* (*SP*) overall only (without the CP analysis grouping).

8.1 Subject disposition

Subject disposition will be represented in tables and listings for *all patients who signed the written patient authorization form* and will include the following results:

- the number of subjects who signed the written patient authorization form;
- the number of subjects in each analyzed population;
- the number of subjects who has HCV RNA assessment on SVR12;
- the number of subjects without HCV RNA assessment on SVR12 and the reasons for it;
- the number of patients with the violations of the eligibility criteria and the corresponding violated inclusion/exclusion criteria.

8.2 Protocol deviations

The presentation of Protocol deviations is not planned in this study.

8.3 Demographic and baseline variables

Tables with descriptive statistics in accordance with section 7.1 will be presented for the following parameters, which are evaluated on visit 1:

- demographics and anthropometric characteristics:
  - gender;
  - race/ethnic origin;
  - height;
  - weight;
  - BMI [weight (kg) / height (m^2)];
- duration of HCV infection diagnosis (in years);
- IL28B genotypes;

[1] Sections 9.6 “Inclusion Criteria” and 9.7 “Exclusion Criteria” of the clinical study Protocol.
[2] Parameter “CIRRHOSIS SCORE” from eCRF form “CHC DISEASE CHARACTERISTICS”.
[3] Parameter “Prior treatment for CHC” from eCRF form “MOST RECENT PRIOR THERAPY FOR CHC”.

- most likely mode of HCV infection;
- liver biopsy results (staging by histopathological scoring system):
  - elastography (kPa);
  - FibroTest;
- presence of esophageal varices;
- history of liver decompensation;
- Child Pugh score;
- alcohol consumption:
  - alcohol use;
  - number of units/drinks per week (for patients who regular use alcohol).

All corresponding listings will be presented.

8.4 Concurrent illnesses and medical conditions

Medical history will be coded using the MedDRA version 20.0 (or further updating) and summarized by system organ class (SOC) and preferred term (PT) according Data MATRIX LLC SOP [3] and will be presented in listings and tables.

Tables with descriptive statistics in accordance with section 7.1 will be presented for the following parameters, which are evaluated on visit 1:

- co-infection information:
  - presence of co-infection with other relevant diseases;
  - CD4 T-cell count (for HIV co-infected patients);
  - HIV-RNA test results (for HIV co-infected patients);
- liver and/or CHC related co-morbidities;
- other co-morbidities.

8.5 Prior and concurrent medications

All medications will be coded using WHODD version Jun 2015 (or actual version on the time of the study completion) according Data MATRIX LLC SOP [3]. Prior and concurrent medications will be presented in a separate listings and tables.

Prior medication will be determined using “MOST RECENT PRIOR THERAPY FOR CHC” flag in the CMCAT variable of CM domain of the database. Concurrent medications will be determined using “CO-MEDICATION” flag in the CMCAT variable of CM domain of the database.

Additionally listings will contain the following information for prior CHC therapy:

- presence of prior treatment for CHC;
- generic drug name;
- initial dose (by generic drug name groups and units groups);
- start frequency (by generic drug name groups);
- duration (by generic drug name groups, in weeks);
- outcome prior treatment.

9 Effectiveness analysis

All analyses of effectiveness will be performed on the TP, CP and CPSFU populations with separate tables for each population as the result. Tables for equal sets (contain exactly the

same patients) will not be presented, equal sets will be pointed in the footnote with description only.

The following effectiveness outcomes will be included in the analyses:

- SVR12 achieving;
- virological response at EoT;
- patients with at least one and each of SVR12 non-response categories:
  - relapse during treatment phase;
  - relapse after EoT;
  - failure to suppress;
  - premature study drug discontinuation with no on-treatment virologic failure;
  - missing SVR12 data.

Due to the fact that in the Russian clinical practice tests for HCV RNA often have limit of detection higher than 50 IU/mL and may vary across laboratories, effectiveness outcomes will be analyzed with the following definitions:

- SVR12 achieving (single last HCV RNA value <50 IU/mL or undetectable/negative 12 weeks after the last actual dose of the ABBVIE REGIMEN);
- virological response (HCV RNA <50 IU/mL or undetectable/negative) at EoT;
- patients with at least one and each of SVR12 non-response categories:
  - relapse during treatment phase (breakthrough, i.e. at least one documented HCV RNA value <50 IU/mL or undetectable/negative followed by HCV RNA value ≥50 IU/mL or positive during treatment);
  - relapse after EoT (HCV RNA value <50 IU/mL or undetectable/negative at EoT or at the last on-treatment HCV RNA measurement followed by HCV RNA ≥50 IU/mL or positive post-treatment);
  - failure to suppress (each measured on-treatment HCV RNA value ≥50 IU/mL or positive);
  - premature study drug discontinuation with no on-treatment virologic failure;
  - missing SVR12 data and/or none of the above criteria.

Figure 9.1 illustrates the patient's distribution by SVR12 response/non-response categories.

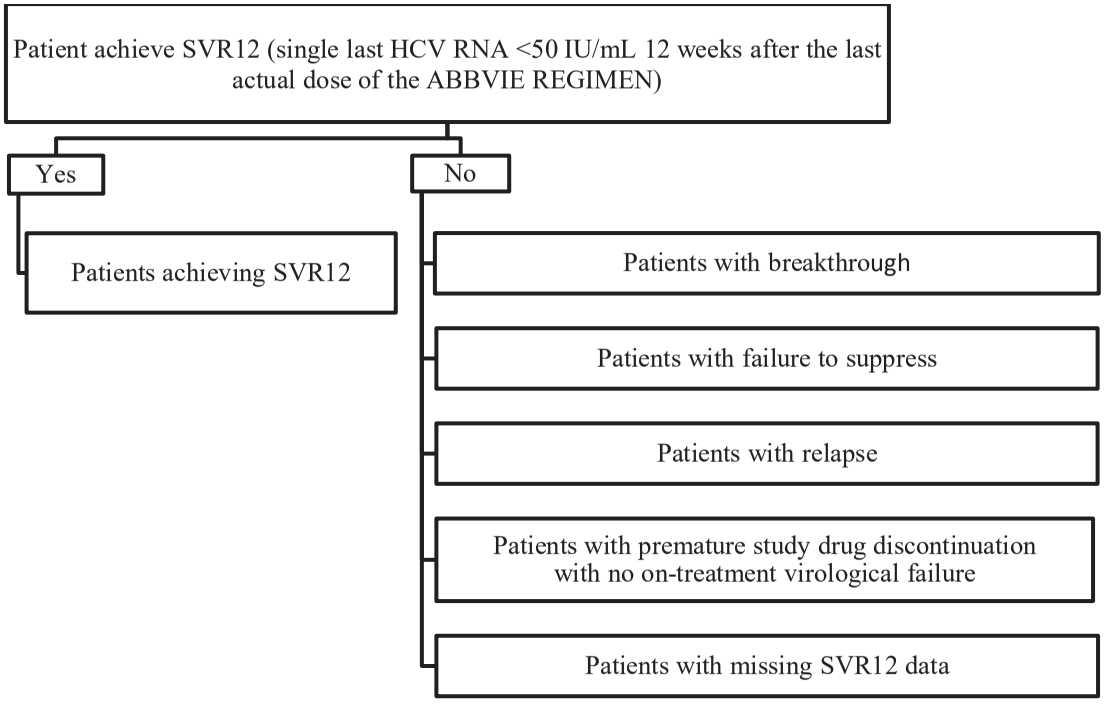

Figure 9.1 – Patient's distribution by SVR12 response/non-response categories

Frequencies and percentages with 95% confidence intervals will be calculated for each effectiveness outcomes and will be presented according the section 7.1. Also frequency tables will be repeated for patients in subgroup without missing SVR12 data category.

Effectiveness endpoints (SVR12 achieving, virological response at EoT and relapse after EoT) will be analyzed using univariate logistic regression, if applicable. These analyses will be of exploratory nature, data driven, and will be repeatedly performed for various CP analysis groups, since not each covariate might be predictive in each patient group.

The following parameters can be included in the univariate models as explanatory variables (fixed effect or covariate):

- treatment experience (with/without prior treatment for CHC);
- Child Pugh score;
- result of FibroTest;
- history of liver decompensation;
- age;
- gender;
- race;
- BMI;
- laboratory hematology[1]:
  - hemoglobin;
  - platelets;
  - prothrombin time;
- laboratory clinical chemistry:
  - ALT;

[1] Note that all Hematology variables and all Clinical Chemistry should be in the same units. If it is impossible to bring units to the same the smallest units groups will be accepted as missing. If it is impossible to identify the smallest units groups the corresponding covariate will be deleted from the analysis.

- AST;
- Gamma-GT;
- total bilirubin;
- albumin;
- creatinine clearance;
- alpha-1-fetoprotein.

Additionally, after univariate model analyses all effectiveness endpoints can be analyzed using MLR (if applicable) which consider only covariates in the selection procedure with a p-value <0.25 in the corresponding univariate logistic regression analysis[1].

To avoid the multicollinearity problem all possible explanatory variables will be examined using following SAS script:

ods graphics on;
PROC CORR data=<dataset> plots=all;
VAR <variables>;
RUN;
ods graphics off;

Statistical significant correlated variables with correlation coefficient ≥ 40 should be considered and managed. All solutions about an explanatory variables choosing will be of exploratory nature, data driven, and will be described with presenting of results of the "*PROC CORR"* SAS procedure.

Backward selection procedures will be applied to generate the final MLR models esing the SAS procedure LOGISTIC with statement SELECTION = BACKWARD and SLENTRY = 0.05. A p-value <0.05 condition will be used for the covariates to stay in the model in a backward elimination step.

Odds ratio with 95% Wild CI, p-values will be presented for each predictor.

All data for effectiveness analyses will be listed in separate listings (for each effectiveness analyses endpoint).

10 Safety analysis

Safety analysis will be conducted on *the safety population* (*SP*).

The following parameters will be analyzed:
– study drug exposure;
– adverse events;
– pregnancies;
– clinical laboratory evaluations.

10.1 Exposure

Tables with descriptive statistics in accordance with section 7.1 will be presented for the following parameters:
– actual duration ABBVIE REGIMEN (in days);

[1] Note that MLR is possible ONLY if more than one explanatory variables will have a p-value <0.25 in the corresponding univariate logistic regression analysis.

- the number of patients with collected deviating duration reasons;
- adherence ABBVIE REGIMEN (calculated for Paritaprevir/R-Ombitasvir and for Dasabuvir separately):
  - percentage of target dose taken in treatment intervals (weeks 1-4, 5-8 and 9-12) for Paritaprevir/R-Ombitasvir and for Dasabuvir;
  - percentage of patients who missed of study drug administration for at least 7 days in a row.

All corresponding listings will be presented.

10.2 Adverse events

Only treatment-emergent adverse events will be analyzed.

Treatment-emergent AE is any reported event that begins or worsens in severity after initiation of study drug through 30 days post-study drug dosing.

All analyzed AEs will be coded using the MedDRA version 20.0 (or further updating) and tabulated in the report with grouping by primary system organ class (SOC) and preferred term (PT).

The frequency of a specific AE occurrence will be presented by the proportion of patients with this AE emergence as well as the total number of episodes this AE for a diagnosis.

The following tables with descriptive statistics in accordance with section 7.1 will be presented:

- all AE / SAE;
- AE / SAE by severity;
- AE / SAE by relationship to the study drug.

Tables of AE/SAE by severity (relationship to the study drug) will be prepared using the following rules. Each SOC / PT category will include only the AEs with the highest severity (relationship to the drug) in each patient, while in the Total category all AEs of this patient will be considered. At the same time, each patient will be counted only once with highest severity (relationship to the study drug) in each SOC and each PT level as well as Total level.

Also all AEs will be presented in listings. Additional listings for unintended medication errors will be provided.

10.3 Pregnancies

Female subjects will be tested for pregnancy at each study visit. The results of these tests and pregnancies episodes will be reported in the listing.

10.4 Clinical laboratory evaluations

Clinical laboratory evaluations include the following parameters:

- hematology results;
- blood chemistry results.

The following parameters, which are evaluated at each study visit, will be analyzed in tables and presented in listings:

- hematology:
  - hemoglobin;
  - platelets;
  - prothrombin time (seconds);

- prothrombin time (INR);

– blood chemistry:
  - ALT;
  - AST;
  - GGT;
  - total bilirubin;
  - alpha-1-fetoprotein;
  - albumin;
  - creatinine;
  - creatinine clearance.

The results of clinical laboratory evaluations statistical analysis will be represented in accordance with section 7.1 as the following outputs:

– tables with descriptive statistics of measurement values and changes from baseline (visit 1);
– frequency tables of out of range and clinically significant evaluates will be presented;
– shift tables based on clinical evaluation of measurements at visit 1.

10.5 Other safety measures

No other safety measures will be analysed in this study.

11 Pharmacokinetics

No pharmacokinetic and pharmacodynamic parameters will be analyzed in this study.

12 Other analyses

No other analyses will be performed in this study.

13 Interim analyses and data monitoring

No interim analysis is planned for this study.

14 Technical details and reporting conventions

Statistical analysis will be performed using SAS 9.4. One (final) statistical analysis report will be prepared in the Microsoft Office Word *(.docx)* format after the end of data collection and database lock. The results of statistical analysis will be presented in the form of tables, figures and listings in English.

15 Summary of changes to the Protocol

This SAP is fully consistent with the clinical study Protocol.

16 List of TFLs

16.1 Tables

Subjects Disposition

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Table 1.1 – Subjects Dispositions
Table 1.2 – The reasons of early wirthdrawal
Table 1.3 – Violation of eligibility criteria
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Demographics and anthropometric characteristics

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Table 1.4.1 – Demographics and anthropometric characteristics [CP]
Table 1.4.2 – Demographics and anthropometric characteristics (prior treatment groups) [CP]
Table 1.4.3 – Demographics and anthropometric characteristics (treatment-experienced groups)
[CP]
Table 1.4.4 – Demographics and anthropometric characteristics (Child Pugh score groups) [CP]
Table 1.4.5 – Demographics and anthropometric characteristics [TP]
Table 1.4.6 – Demographics and anthropometric characteristics [SP]
```

CHC disease characteristics

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Table 1.5.1 – CHC disease characteristics [CP]
Table 1.5.2 – CHC disease characteristics (prior treatment groups) [CP]
Table 1.5.3 – CHC disease characteristics (treatment-experienced groups) [CP]
Table 1.5.4 – CHC disease characteristics (Child Pugh score groups) [CP]
Table 1.5.5 – CHC disease characteristics [TP]
Table 1.5.6 – CHC disease characteristics [SP]
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Liver fibrosis stage

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Table 1.6.1 – Liver fibrosis stage [CP]
Table 1.6.2 – Liver fibrosis stage (prior treatment groups) [CP]
Table 1.6.3 – Liver fibrosis stage (treatment-experienced groups) [CP]
Table 1.6.4 – Liver fibrosis stage (Child Pugh score groups) [CP]
Table 1.6.5 – Liver fibrosis stage [TP]
Table 1.6.6 – Liver fibrosis stage [SP]
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Alcohol consumption

Table 1.7.1 – Alcohol consumption [CP]
Table 1.7.2 – Alcohol consumption (prior treatment groups) [CP]
Table 1.7.3 – Alcohol consumption (treatment-experienced groups) [CP]
Table 1.7.4 – Alcohol consumption (Child Pugh score groups) [CP]
Table 1.7.5 – Alcohol consumption [TP]
Table 1.7.6 – Alcohol consumption [SP]

Liver and/or CHC related co-morbidities

Table 1.8.1 – Liver and/or CHC related co-morbidities [CP]
Table 1.8.2 – Liver and/or CHC related co-morbidities (prior treatment groups) [CP]
Table 1.8.3 – Liver and/or CHC related co-morbidities (treatment-experienced groups) [CP]
Table 1.8.4 – Liver and/or CHC related co-morbidities (Child Pugh score groups) [CP]
Table 1.8.5 – Liver and/or CHC related co-morbidities [TP]
Table 1.8.6 – Liver and/or CHC related co-morbidities [SP]

Other co-morbidities

Table 1.9.1 – Other co-morbidities [CP]
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Table 1.9.3 – Other co-morbidities (treatment-experienced groups) [CP]
Table 1.9.4 – Other co-morbidities (Child Pugh score groups) [CP]
Table 1.9.5 – Other co-morbidities [TP]
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Co-infections

Table 1.10.1 – Co-infections [CP]
Table 1.10.2 – Co-infections (prior treatment groups) [CP]
Table 1.10.3 – Co-infections (treatment-experienced groups) [CP]
Table 1.10.4 – Co-infections (Child Pugh score groups) [CP]
Table 1.10.5 – Co-infections [TP]
Table 1.10.6 – Co-infections [SP]

HIV most recent test results

Table 1.11.1 – HIV most recent test results [CP]
Table 1.11.2 – HIV most recent test results (prior treatment groups) [CP]
Table 1.11.3 – HIV most recent test results (treatment-experienced groups) [CP]
Table 1.11.4 – HIV most recent test results (Child Pugh score groups) [CP]
Table 1.11.5 – HIV most recent test results [TP]
Table 1.11.6 – HIV most recent test results [SP]

Prior Medications for CHC

Table 1.12.1 – Prior Medications for CHC [CP]
Table 1.12.2 – Prior Medications for CHC (prior treatment groups) [CP]
Table 1.12.3 – Prior Medications for CHC (treatment-experienced groups) [CP]
Table 1.12.4 – Prior Medications for CHC (Child Pugh score groups) [CP]
Table 1.12.5 – Prior Medications for CHC [TP]
Table 1.12.6 – Prior Medications for CHC [SP]

Concurrent Medications for CHC

Table 1.13.1 – Concurrent Medications for CHC [CP]
Table 1.13.2 – Concurrent Medications for CHC (prior treatment groups) [CP]
Table 1.13.3 – Concurrent Medications for CHC (treatment-experienced groups) [CP]
Table 1.13.4 – Concurrent Medications for CHC (Child Pugh score groups) [CP]
Table 1.13.5 – Concurrent Medications for CHC [TP]
Table 1.13.6 – Concurrent Medications for CHC [SP]

Effectiveness analysis

Table 2.1.1.1 – Percentage for effectiveness endpoints [TP]
Table 2.1.1.2 – Percentage for effectiveness endpoints in subgroup without missing SVR12 data [TP]

Table 2.1.X.1 – SVR12 achieving. Univariate logistic regression results [TP]
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Table 2.1.X.1 – Virological response at EoT. Univariate logistic regressions results [TP]
Table 2.1.X.2 – Virological response at EoT. Multiple logistic regression results [TP]
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Table 2.1.X.2 – Relapse after EoT. Multiple logistic regression results [TP]

Table 2.2.1.1 – Percentage for effectiveness endpoints [CP]
Table 2.2.1.2 – Percentage for effectiveness endpoints in subgroup without missing SVR12 data [CP]

Table 2.2.X.1 – SVR12 achieving. Univariate logistic regression results [TP]
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Table 2.2.X.1 – Virological response at EoT. Univariate logistic regressions results [TP]
Table 2.2.X.2 – Virological response at EoT. Multiple logistic regression results [TP]
Table 2.2.X.1 – Relapse after EoT. Univariate logistic regressions results [TP]
Table 2.2.X.2 – Relapse after EoT. Multiple logistic regression results [TP]

Table 2.3.1.1 – Percentage for effectiveness endpoints [CPSFU]
Table 2.3.1.2 – Percentage for effectiveness endpoints in subgroup without missing SVR12 data [CPSFU]

Table 2.3.X.1 – SVR12 achieving. Univariate logistic regression results [CPSFU]
Table 2.3.X.2 – SVR12 achieving. Multiple logistic regression results [CPSFU]
Table 2.3.X.1 – Virological response at EoT. Univariate logistic regressions results [CPSFU]
Table 2.3.X.2 – Virological response at EoT. Multiple logistic regression results [CPSFU]
Table 2.3.X.1 – Relapse after EoT. Univariate logistic regressions results [CPSFU]
Table 2.3.X.2 – Relapse after EoT. Multiple logistic regression results [CPSFU]

Exposure
Table 3.1 – AbbVie REGIMEN intake

Adverse events
Table 3.2.1 – Adverse events
Table 3.2.2 – Serious adverse events
Table 3.2.3 – Adverse events by relationship to the study drug
Table 3.2.4 – Serious adverse events by relationship to the study drug
Table 3.2.5 – Adverse events by severity
Table 3.2.6 – Serious adverse events by severity

Hematology
Table 3.3.1 – Hematology. Descriptive statistics
Table 3.3.2 – Hematology. Clinical assessments
Table 3.3.3 – Hematology. Shift table

Blood chemistry
Table 3.4.1 – Blood chemistry. Descriptive statistics
Table 3.4.2 – Blood chemistry. Clinical assessments
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16.2 Figures

No figures are planned in the study.

16.3 Listings

Patients disposition
Listing 1.1 – Disposition: analysis populations
Listing 1.2 – Disposition: subject visits
Listing 1.3 – Disposition: study completion
Listing 1.4 – Violation of inclusion/exclusion criteria

Demographics and baseline characteristics
Listing 2.1 – Demographics and anthropometric characteristics
Listing 2.2 – CHC disease characteristics
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Effectiveness analysis

Listing 3.1 – HCV RNA

Safety analysis

Listing 4.1 – Adverse Events
Listing 4.2.1 – ABBVIE REGIMEN: exposure
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Listing 4.3 – Pregnancy
Listing 4.4 – Hematology results
Listing 4.5.1 – Blood chemistry results
Listing 4.5.2 – Optional blood chemistry results

17 References

1) Committee for Proprietary Medicinal Products (CPMP). International Conference on Harmonisation (ICH) Topic E9: Note for Guidance on Statistical Principles for Clinical Trials; September 1998.
2) DataMatrix_SOP_STAT001_Statistical Principles_ver.2.0_June 2016.
3) DataMatrix_SOP_DM010_Dictionary Management and Data Coding_ver.2.0_August 2015.

18 Tables shells

Subjects disposition

AbbVie LLC
P16-253 (CITRIN)
Table 1.1 Subjects Disposition
All patients
Page X of X

	Total n (%)
Subjects who signed the written patient authorization form	XX
The target population (TP)	XX (XX.X)
The core population (TP)	XX (XX.X)
The safety population (SP)	XX (XX.X)
The non-core population (NCP)	XX (XX.X)
The core population with sufficient follow-up data (CPSFU)	XX (XX.X)

n: the number of subjects within a specific category.
Percentages were calculated from the number of subjects who signed the written patient authorization form.

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.2 The reasons of early withdrawal
The target population
Page X of X

	Total (N = XX) n (%)
Subjects with HCV RNA assessment on SVR12	XX (XX.X)
Subjects without HCV RNA assessment on SVR12	XX (XX.X)
Reason if HCV RNA assessment on SVR12 not done:	
Failure to return	XX (XX.X)
Insufficient virological response	XX (XX.X)
Withdrawn consent	XX (XX.X)
Death	XX (XX.X)
...	...

N: the number of subjects in the target population. n: the number of subjects within a specific category. Percentages were calculated as (100 x n/N).

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.3 Violation of eligibility criteria
The target population
Page X of X

	Total (N = XX) n (%)
Patients with violation of inclusion criteria	XX (XX.X)
Inclusion criterion #1	XX (XX.X)
Inclusion criterion #2	XX (XX.X)
...	...
Patients with violation of exclusion criteria	XX (XX.X)
Exclusion criterion #1	XX (XX.X)
Exclusion criterion #2	XX (XX.X)
...	...
Subject has fulfilled all the inclusion and does not meet any exclusion criteria and is eligible for the trial	XX (XX.X)

N: the number of subjects in the target population. n: the number of subjects within a specific category. Percentages are calculated as (100 x n/N).

Program code, date, time

Data extracted: DD.MM.YYYY

Demographic and anthropometric characteristics

AbbVie LLC
P16-253 (CITRIN)
Table 1.4.1 Demographics and anthropometric characteristics
The core population
Page X of X

		Total (N=XX)
Age (years)		
n		XX
Mean		XX.X
SD		XX.XX
Median		XX.X
IQR		XX.X
Min		XX
Max		XX
Gender		
n		XX
Male	n (%)	XX (XX.X)
Female	n (%)	XX (XX.X)
Race		
n		XX
White/Caucasian	n (%)	XX (XX.X)
Black	n (%)	XX (XX.X)
Asian/Oriental	n (%)	XX (XX.X)
Native American/American Indian	n (%)	XX (XX.X)
Other	n (%)	XX (XX.X)
Weight (kg)		
...		...
Height (cm)		
...		...
BMI (kg/m^2)		
...		...

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).
IQR: interquartile range. Body Mass Index (BMI): weight (kg) / [height (m)^2].
Age is calculated as the number of full years between the date of birth and the date of signing the written patient authorization form.

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.4.2 Demographics and anthropometric characteristics (prior treatment groups)
The core population
Page X of X

		Treatment-experienced (N=XX)	Naïve (N=XX)
Age (years)			
...		...	...
Gender			
...	...	...	...
Race			
...	...	...	...
Weight (kg)			
...		...	...
Height (cm)			
...		...	...
BMI (kg/m^2)			
...		...	...

N: the number of subjects in the prior treatment groups of the core population. n: the number of valid measurements.
IQR: interquartile range. Body Mass Index (BMI): weight (kg) / [height (m)^2]. Percentages are calculated as (100 x n/N).
Age is calculated as the number of full years between the date of birth and the date of signing the written patient authorization form.

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)

Table 1.4.3 Demographics and anthropometric characteristics (treatment-experienced groups)

The core population
Page X of X

		PEG-INF alpha (N=XX)	non-PEG-INF alpha (N=XX)	INF all (N=XX)	Ribavirin (N=XX)
Age (years)					
...		...	...	...	...
Gender					
...	...	...	...	...	...
Race					
...	...	...	...	...	...
Weight (kg)					
...		...	...	...	...
Height (cm)					
...		...	...	...	...
BMI (kg/m^2)					
...		...	...	...	...

N: the number of subjects in the treatment-experienced groups of the core population. n: the number of valid measurements.
IQR: interquartile range. Body Mass Index (BMI): weight (kg) / [height (m)^2]. Percentages are calculated as (100 x n/N).
PEG-INF alpha: Pegylated Interferon alpha. non-PEG-INF alpha: Interferon alpha (non-pegylated).
Age is calculated as the number of full years between the date of birth and the date of signing the written patient authorization form.

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.4.4 Demographics and anthropometric characteristics (Child Pugh score groups)
The core population
Page X of X

		Score 5 (N=XX)	Score 6 (N=XX)
Age (years)			
...		...	...
Gender			
...	...	...	...
Race			
...	...	...	...
Weight (kg)			
...		...	...
Height (cm)			
...		...	...
BMI (kg/m^2)			
...		...	...

N: the number of subjects in the Child Pugh score groups of the core population. n: the number of valid measurements.
IQR: interquartile range. Body Mass Index (BMI): weight (kg) / [height (m)^2]. Percentages are calculated as (100 x n/N).
Age is calculated as the number of full years between the date of birth and the date of signing the written patient authorization form.

Program code, date, time Data extracted: DD.MM.YYYY

Similar to table 1.4.1, tables for the target and the safety populations will be constructed:

Table 1.4.5 Demographics and anthropometric characteristics
Table 1.4.6 Demographics and anthropometric characteristics

CHC disease characteristics

AbbVie LLC
P16-253 (CITRIN)
Table 1.5.1 CHC disease characteristics
The core population
Page X of X

		Total (N=XX)
Duration of HCV infection diagnosis (in years)		
n		XX
Mean		XX.X
SD		XX.XX
Median		XX.X
IQR		XX.X
Min		XX
Max		XX
Most likely mode of HCV infection		
n		XX
Blood transfusions	n (%)	XX (XX.X)
Dental procedures	n (%)	XX (XX.X)
...	...	...
IL28B genotypes		
rs12979860		
n		XX
CC	n (%)	XX (XX.X)
CT	n (%)	XX (XX.X)
TT	n (%)	XX (XX.X)
Unknown	n (%)	XX (XX.X)
rs8099917		
n		XX
GG	n (%)	XX (XX.X)
TG	n (%)	XX (XX.X)
TT	n (%)	XX (XX.X)
Unknown	n (%)	XX (XX.X)

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.5.2 CHC disease characteristics (prior treatment groups)
The core population
Page X of X

		Treatment-experienced (N=XX)	Naïve (N=XX)
Duration of HCV infection diagnosis (in years)			
...		...	...
Most likely mode of HCV infection			
...	...	...	...
IL28B genotypes			
rs12979860			
...	...	...	...
rs8099917			
...	...	...	...

N: the number of subjects in the prior treatment groups of the core population.
n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.5.3 CHC disease characteristics (treatment-experienced groups)
The core population
Page X of X

	PEG-INF alpha (N=XX)	non-PEG-INF alpha (N=XX)	INF all (N=XX)	Ribavirin (N=XX)
Duration of HCV infection diagnosis (in years)				
...	...	...	...	...
Most likely mode of HCV infection				
...	...	...	...	...
IL28B genotypes				
rs12979860				
...	...	...	...	...
rs8099917				
...	...	...	...	...

N: the number of subjects in the prior treatment groups of the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).
PEG-INF alpha: Pegylated Interferon alpha. non-PEG-INF alpha: Interferon alpha (non-pegylated).

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.5.4 CHC disease characteristics (Child Pugh score groups)
The core population
Page X of X

		Score 5 (N=XX)	Score 6 (N=XX)
Duration of HCV infection diagnosis (in years)			
...		...	...
Most likely mode of HCV infection			
...	...	...	...
IL28B genotypes			
rs12979860			
...	...	...	...
rs8099917			
...	...	...	...

N: the number of subjects in the prior treatment groups of the core population.
n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time Data extracted: DD.MM.YYYY

Similar to table 1.5.1, tables for the target and the safety populations will be constructed:

Table 1.5.5 CHC disease characteristics
Table 1.5.6 CHC disease characteristics

Liver fibrosis stage

AbbVie LLC
P16-253 (CITRIN)
Table 1.6.1 Liver fibrosis stage
The core population
Page X of X

	Total (N=XX) n (%)
Staging by histopathological scoring system	
Elastography (kPa)	
n	XX
<8.8	XX (XX.X)
8.8-<9.6	XX (XX.X)
9.6-<14.6	XX (XX.X)
>=14.6	XX (XX.X)
FibroTest	
n	XX
<=0.21	XX (XX.X)
0.22-0.27	XX (XX.X)
0.28-0.31	XX (XX.X)
...	...
Presence of esophageal varices	
n	XX
Yes	XX (XX.X)
No	XX (XX.X)
Unknown	XX (XX.X)
History of liver decompensation	
n	XX
No, never decompensated	XX (XX.X)
Yes, but currently compensated	XX (XX.X)
Child Pugh score	
n	XX
5	XX (XX.X)
6	XX (XX.X)
...	...

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.6.2 Liver fibrosis stage (prior treatment groups)
The core population
Page X of X

	Treatment-experienced (N=XX) n (%)	Naïve (N=XX) n (%)
Staging by histopathological scoring system		
Elastography (kPa)		
...	...	...
FibroTest		
...	...	...
Presence of esophageal varices		
...	...	...
History of liver decompensation		
...	...	...
Child Pugh score		
...	...	...

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.6.3 Liver fibrosis stage (treatment-experienced groups)
The core population
Page X of X

	PEG-INF alpha (N=XX) n (%)	non-PEG-INF alpha (N=XX) n (%)	INF all (N=XX) n (%)	Ribavirin (N=XX) n (%)
Staging by histopathological scoring system				
Elastography (kPa)				
...	...	...	...	...
FibroTest				
...	...	...	...	...
Presence of esophageal varices				
...	...	...	...	...
History of liver decompensation				
...	...	...	...	...
Child Pugh score				
...	...	...	...	...

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).
PEG-INF alpha: Pegylated Interferon alpha. non-PEG-INF alpha: Interferon alpha (non-pegylated).

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.6.4 Liver fibrosis stage (Child Pugh score groups)
The core population
Page X of X

	Score 5 (N=XX) n (%)	Score 6 (N=XX) n (%)
Staging by histopathological scoring system		
Elastography (kPa)		
...	...	...
FibroTest		
...	...	...
Presence of esophageal varices		
...	...	...
History of liver decompensation		
...	...	...

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time Data extracted: DD.MM.YYYY

Similar to table 1.6.1, tables for the target and the safety populations will be constructed:

Table 1.6.5 Liver fibrosis stage
Table 1.6.6 Liver fibrosis stage

Alcohol consumption

AbbVie LLC
P16-253 (CITRIN)
Table 1.7.1 Alcohol consumption
The core population
Page X of X

		Total (N=XX)
Alcohol use		
n		XX
Ex-drinker	n (%)	XX (XX.X)
None	n (%)	XX (XX.X)
Yes, occasional	n (%)	XX (XX.X)
Yes, regular	n (%)	XX (XX.X)
Number of units/drinks per week		
n		XX
Mean		XX.X
SD		XX.XX
Median		XX.X
IQR		XX.X
Min		XX
Max		XX

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.7.2 Alcohol consumption (prior treatment groups)
The core population
Page X of X

		Treatment-experienced (N=XX)	Naïve (N=XX)
Alcohol use			
n		XX	XX
Ex-drinker	n (%)	XX (XX.X)	XX (XX.X)
None	n (%)	XX (XX.X)	XX (XX.X)
Yes, occasional	n (%)	XX (XX.X)	XX (XX.X)
Yes, regular	n (%)	XX (XX.X)	XX (XX.X)
Number of units/drinks per week			
n		XX	XX
Mean		XX.X	XX.X
SD		XX.XX	XX.XX
Median		XX.X	XX.X
IQR		XX.X	XX.X
Min		XX	XX
Max		XX	XX

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)

Table 1.7.3 Alcohol consumption (treatment-experienced groups)

The core population
Page X of X

		PEG-INF alpha (N=XX)	non-PEG-INF alpha (N=XX)	INF all (N=XX)	Ribavirin (N=XX)
Alcohol use					
n		XX	XX	XX	XX
Ex-drinker	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
None	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Yes, occasional	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Yes, regular	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of units/drinks per week					
n		XX	XX	XX	XX
Mean		XX.X	XX.X	XX.X	XX.X
SD		XX.XX	XX.XX	XX.XX	XX.XX
Median		XX.X	XX.X	XX.X	XX.X
IQR		XX.X	XX.X	XX.X	XX.X
Min		XX	XX	XX	XX
Max		XX	XX	XX	XX

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).
PEG-INF alpha: Pegylated Interferon alpha. non-PEG-INF alpha: Interferon alpha (non-pegylated).

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.7.4 Alcohol consumption (Child Pugh score groups)
The core population
Page X of X

		Score 5 (N=XX)	Score 6 (N=XX)
Alcohol use			
n		XX	XX
Ex-drinker	n (%)	XX (XX.X)	XX (XX.X)
None	n (%)	XX (XX.X)	XX (XX.X)
Yes, occasional	n (%)	XX (XX.X)	XX (XX.X)
Yes, regular	n (%)	XX (XX.X)	XX (XX.X)
Number of units/drinks per week			
n		XX	XX
Mean		XX.X	XX.X
SD		XX.XX	XX.XX
Median		XX.X	XX.X
IQR		XX.X	XX.X
Min		XX	XX
Max		XX	XX

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time Data extracted: DD.MM.YYYY

Similar to table 1.7.1, tables for the target and the safety populations will be constructed:

Table 1.7.5 Alcohol consumption
Table 1.7.6 Alcohol consumption

Medical history

AbbVie LLC
P16-253 (CITRIN)
Table 1.8.1 Liver and/or CHC related co-morbidities
The core population
Page X of X

System Organ Class Preferred Term [1]	Total (N=XX) n (%) / E
Overall	XX (XX.X) / XX
System Organ Class 1	XX (XX.X) / XX
Preferred Term A	XX (XX.X) / XX
Preferred Term A	XX (XX.X) / XX
...	...
System Organ Class 2	XX (XX.X) / XX
Preferred Term C	XX (XX.X) / XX
Preferred Term D	XX (XX.X) / XX
...	...
...	...

N: the number of subjects in the core population. n: the number of subjects within a specific category. E: number of medical history events reported.
Liver and/or chc related co-morbidities were coded using MedDRA 20.1. Percentages are calculated from the number of subjects in the core population.
System organ classes (SOC) and preferred terms (PT) within each SOC are sorted in descending order of Total frequency count.
[1] Within SOC patients may have reported more than one PT.

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.8.2 Liver and/or CHC related co-morbidities (prior treatment groups)
The core population
Page X of X

System Organ Class Preferred Term [1]	Treatment-experienced (N=XX) n (%) / E	Naïve (N=XX) n (%) / E
Overall	XX (XX.X) / XX	XX (XX.X) / XX
System Organ Class 1	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term A	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term A	XX (XX.X) / XX	XX (XX.X) / XX
...	...	...
System Organ Class 2	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term C	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term D	XX (XX.X) / XX	XX (XX.X) / XX
...	...	...
...	...	...

N: the number of subjects in the core population. n: the number of subjects within a specific category. E: number of medical history events reported.
Liver and/or chc related co-morbidities were coded using MedDRA 20.1. Percentages are calculated from the number of subjects in the core population.
System organ classes (SOC) and preferred terms (PT) within each SOC are sorted in descending order of Treatment-experienced frequency count.
[1] Within SOC patients may have reported more than one PT.

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)

Table 1.8.2 Liver and/or CHC related co-morbidities (treatment-experienced groups)

The core population
Page X of X

System Organ Class Preferred Term [1]	PEG-INF alpha (N=XX) n (%) / E	non-PEG-INF alpha (N=XX) n (%) / E	INF all (N=XX) n (%) / E	Ribavirin (N=XX) n (%) / E
Overall	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX
System Organ Class 1	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term A	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term A	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX
...	...	...	...	...
System Organ Class 2	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term C	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term D	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX	XX (XX.X) / XX
...	...	...	...	...
...	...	...	...	...

N: the number of subjects in the core population. n: the number of subjects within a specific category. E: number of medical history events reported.
PEG-INF alpha: Pegylated Interferon alpha. non-PEG-INF alpha: Interferon alpha (non-pegylated).
Liver and/or chc related co-morbidities were coded using MedDRA 20.1. Percentages are calculated from the number of subjects in the core population.
System organ classes (SOC) and preferred terms (PT) within each SOC are sorted in descending order of INF all frequency count.
[1] Within SOC patients may have reported more than one PT.

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.8.2 Liver and/or CHC related co-morbidities (Child Pugh score groups)
The core population
Page X of X

System Organ Class Preferred Term [1]	Score 5 (N=XX) n (%) / E	Score 6 (N=XX) n (%) / E
Overall	XX (XX.X) / XX	XX (XX.X) / XX
System Organ Class 1	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term A	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term A	XX (XX.X) / XX	XX (XX.X) / XX
...	...	...
System Organ Class 2	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term C	XX (XX.X) / XX	XX (XX.X) / XX
Preferred Term D	XX (XX.X) / XX	XX (XX.X) / XX
...	...	...
...	...	...

N: the number of subjects in the core population. n: the number of subjects within a specific category. E: number of medical history events reported.
Liver and/or chc related co-morbidities were coded using MedDRA 20.1. Percentages are calculated from the number of subjects in the core population.
System organ classes (SOC) and preferred terms (PT) within each SOC are sorted in descending order of score 5 frequency count.
[1] Within SOC patients may have reported more than one PT.

Program code, date, time Data extracted: DD.MM.YYYY

Similar to table 1.8.1, tables for the target and the safety populations will be constructed:

Table 1.8.5 Liver and/or CHC related co-morbidities
Table 1.8.6 Liver and/or CHC related co-morbidities

Similar to tables 1.8.X, tables for the other co-morbidities will be constructed:

for the core population

Table 1.9.1 Other co-morbidities
Table 1.9.2 Other co-morbidities (prior treatment groups)
Table 1.9.3 Other co-morbidities (treatment-experienced groups)
Table 1.9.4 Other co-morbidities (Child Pugh score groups)

for the target and safety populations

Table 1.9.5 Other co-morbidities
Table 1.9.6 Other co-morbidities

Co-infections

AbbVie LLC
P16-253 (CITRIN)
Table 1.10.1 Co-infections
The core population
Page 1 of 1

Diagnosis	Total (N=XX) n (%)
Hepatitis B	XX (XX.X)
Human immunodeficiency virus(HIV)	XX (XX.X)
Tuberculosis	XX (XX.X)
Schistosomiasis	XX (XX.X)

N: the number of subjects in the core population. n: the number of subjects within a specific category. Percentages are calculated as (100 x n/N).

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.10.2 Co-infections (prior treatment groups)
The core population
Page 1 of 1

Diagnosis	Treatment-experienced (N=XX) n (%)	Naïve (N=XX) n (%)
Hepatitis B	XX (XX.X)	
Human immunodeficiency virus(HIV)	XX (XX.X)	
Tuberculosis	XX (XX.X)	
Schistosomiasis	XX (XX.X)	

N: the number of subjects in the core population. n: the number of subjects within a specific category. Percentages are calculated as (100 x n/N).

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.10.3 Co-infections (treatment-experienced groups)
The core population
Page 1 of 1

Diagnosis	PEG-INF alpha (N=XX) n (%)	non-PEG-INF alpha (N=XX) n (%)	INF all (N=XX) n (%)	Ribavirin (N=XX) n (%)
Hepatitis B	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Human immunodeficiency virus(HIV)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Tuberculosis	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Schistosomiasis	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

N: the number of subjects in the core population. n: the number of subjects within a specific category. Percentages are calculated as (100 x n/N).
PEG-INF alpha: Pegylated Interferon alpha. non-PEG-INF alpha: Interferon alpha (non-pegylated).

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.10.4 Co-infections (Child Pugh score groups)
The core population
Page 1 of 1

Diagnosis	Score 5 (N=XX) n (%)	Score 6 (N=XX) n (%)
Hepatitis B	XX (XX.X)	XX (XX.X)
Human immunodeficiency virus(HIV)	XX (XX.X)	XX (XX.X)
Tuberculosis	XX (XX.X)	XX (XX.X)
Schistosomiasis	XX (XX.X)	XX (XX.X)

N: the number of subjects in the core population. n: the number of subjects within a specific category. Percentages are calculated as (100 x n/N).

Program code, date, time Data extracted: DD.MM.YYYY

Similar to table 1.10.1, tables for the target and the safety populations will be constructed:

Table 1.10.5 Co-infections
Table 1.10.6 Co-infections

AbbVie LLC
P16-253 (CITRIN)
Table 1.11.1 HIV most recent test results
The core population
Page X of X

		Total (N=XX)
CD4 T-cell count		
n		XX
less 50	n (%)	XX (XX.X)
50-199	n (%)	XX (XX.X)
200-349	n (%)	XX (XX.X)
350-500	n (%)	XX (XX.X)
>500	n (%)	XX (XX.X)
HIV-RNA test		
Result		
n		XX
undetectable	n (%)	XX (XX.X)
detectable	n (%)	XX (XX.X)
Below limit of quantification		
n		XX
Yes	n (%)	XX (XX.X)
No	n (%)	XX (XX.X)
Quantitative result (unit measure)		
n		XX
Mean		XX.X
SD		XX.XX
Median		XX.X
IQR		XX.X
Min		XX
Max		XX

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)

Table 1.11.2 HIV most recent test results (prior treatment groups)

The core population
Page X of X

		Treatment-experienced (N=XX) n (%)	Naïve (N=XX) n (%)
CD4 T-cell count			
n		XX	XX
less 50	n (%)	XX (XX.X)	XX (XX.X)
50-199	n (%)	XX (XX.X)	XX (XX.X)
200-349	n (%)	XX (XX.X)	XX (XX.X)
350-500	n (%)	XX (XX.X)	XX (XX.X)
>500	n (%)	XX (XX.X)	XX (XX.X)
HIV-RNA test			
Result			
n		XX	XX
undetectable	n (%)	XX (XX.X)	XX (XX.X)
detectable	n (%)	XX (XX.X)	XX (XX.X)
Below limit of quantification			
n		XX	XX
Yes	n (%)	XX (XX.X)	XX (XX.X)
No	n (%)	XX (XX.X)	XX (XX.X)
Quantitative result (unit measure)			
n		XX	XX
Mean		XX.X	XX.X
SD		XX.XX	XX.XX
Median		XX.X	XX.X
IQR		XX.X	XX.X
Min		XX	XX
Max		XX	XX

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.11.3 HIV most recent test results (Child Pugh score groups)
The core population
Page X of X

		PEG-INF alpha (N=XX)	non-PEG-INF alpha (N=XX)	INF all (N=XX)	Ribavirin (N=XX)
CD4 T-cell count					
n		XX	XX	XX	XX
less 50	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
50-199	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
200-349	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
350-500	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
>500	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
HIV-RNA test					
Result					
n		XX	XX	XX	XX
undetectable	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
detectable	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Below limit of quantification					
n		XX	XX	XX	XX
Yes	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
No	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Quantitative result (unit measure)					
n		XX	XX	XX	XX
Mean		XX.X	XX.X	XX.X	XX.X
SD		XX.XX	XX.XX	XX.XX	XX.XX
Median		XX.X	XX.X	XX.X	XX.X
IQR		XX.X	XX.X	XX.X	XX.X
Min		XX	XX	XX	XX
Max		XX	XX	XX	XX

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).
PEG-INF alpha: Pegylated Interferon alpha. non-PEG-INF alpha: Interferon alpha (non-pegylated).

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.11.4 HIV most recent test results (prior treatment groups)
The core population
Page X of X

		Score 5 (N=XX)	Score 6 (N=XX)
CD4 T-cell count			
n		XX	XX
less 50	n (%)	XX (XX.X)	XX (XX.X)
50-199	n (%)	XX (XX.X)	XX (XX.X)
200-349	n (%)	XX (XX.X)	XX (XX.X)
350-500	n (%)	XX (XX.X)	XX (XX.X)
>500	n (%)	XX (XX.X)	XX (XX.X)
HIV-RNA test			
Result			
n		XX	XX
undetectable	n (%)	XX (XX.X)	XX (XX.X)
detectable	n (%)	XX (XX.X)	XX (XX.X)
Below limit of quantification			
n		XX	XX
Yes	n (%)	XX (XX.X)	XX (XX.X)
No	n (%)	XX (XX.X)	XX (XX.X)
Quantitative result (unit measure)			
n		XX	XX
Mean		XX.X	XX.X
SD		XX.XX	XX.XX
Median		XX.X	XX.X
IQR		XX.X	XX.X
Min		XX	XX
Max		XX	XX

N: the number of subjects in the core population. n: the number of valid measurements. Percentages are calculated as (100 x n/N).

Program code, date, time

Data extracted: DD.MM.YYYY

Similar to table 1.11.1, tables for the target and the safety populations will be constructed:

Table 1.11.5 HIV most recent test results
Table 1.11.6 HIV most recent test results

Prior and concurrent medications

AbbVie LLC
P16-253 (CITRIN)
Table 1.12.1 Prior Medications for CHC
The core population
Page X of X

Pharmacological subgroup WHODD chemical substance	Total (N=XX) n (%) /E
Total [1]	XX (XX.X) /XX
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX
XXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX
XXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX
...	...
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX
XXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX
...	...
...	...

N: the number of subjects in the core population. n: the number of subjects within a specific category. Percentages are calculated as (100 x n/N).
E: number of medical history events reported. Prior medications were coded using WHODD version Jun 2015. Each subject is only counted once per preferred name and once per ATC group. ATC group and preferred names within each ATC group are sorted in descending order of Total frequency count.
[1] The Total line displays the number (n) and the proportion (%) of patients, who have at least one prior medication prescription, and the total number of prior medication prescriptions.

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.12.2 Prior Medications for CHC (prior treatment groups)
The core population
Page X of X

Pharmacological subgroup WHODD chemical substance	Treatment-experienced (N=XX) n (%) / E	Naïve (N=XX) n (%) / E
Total [1]	XX (XX.X) /XX	
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX	
XXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX	
XXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX	
...	...	
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX	
XXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX	
...	...	
...	...	

N: the number of subjects in the core population. n: the number of subjects within a specific category. Percentages are calculated as (100 x n/N).
E: number of medical history events reported. Prior medications were coded using WHODD version Jun 2015. Each subject is only counted once per preferred name and once per ATC group. ATC group and preferred names within each ATC group are sorted in descending order of Treatment-experienced frequency count.
[1] The Total line displays the number (n) and the proportion (%) of patients, who have at least one prior medication prescription, and the total number of prior medication prescriptions.

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.12.3 Prior Medications for CHC (treatment-experienced groups)
The core population
Page X of X

Pharmacological subgroup WHODD chemical substance	PEG-INF alpha (N=XX) n (%) / E	non-PEG-INF alpha (N=XX) n (%) / E	INF all (N=XX) n (%) / E	Ribavirin (N=XX) n (%) / E
Total [1]	XX (XX.X) /XX			
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX			
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX			
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX			
...	...			
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX			
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX			
...	...			
...	...			

N: the number of subjects in the core population. n: the number of subjects within a specific category. Percentages are calculated as (100 x n/N).
PEG-INF alpha: Pegylated Interferon alpha. non-PEG-INF alpha: Interferon alpha (non-pegylated).
E: number of medical history events reported. Prior medications were coded using WHODD version Jun 2015. Each subject is only counted once per preferred name and once per ATC group. ATC group and preferred names within each ATC group are sorted in descending order of INF all frequency count.
[1] The Total line displays the number (n) and the proportion (%) of patients, who have at least one prior medication prescription, and the total number of prior medication prescriptions.

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 1.12.4 Prior Medications for CHC (Child Pugh score groups)
The core population
Page X of X

Pharmacological subgroup WHODD chemical substance	Score 5 (N=XX) n (%) / E	Score 6 (N=XX) n (%) / E
Total [1]	XX (XX.X) /XX	
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX	
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX	
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX	
...	...	
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX	
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX (XX.X) /XX	
...	...	
...	...	

N: the number of subjects in the core population. n: the number of subjects within a specific category. Percentages are calculated as (100 x n/N).
E: number of medical history events reported. Prior medications were coded using WHODD version Jun 2015. Each subject is only counted once per preferred name and once per ATC group. ATC group and preferred names within each ATC group are sorted in descending order of score 5 frequency count.
[1] The Total line displays the number (n) and the proportion (%) of patients, who have at least one prior medication prescription, and the total number of prior medication prescriptions.

Program code, date, time Data extracted: DD.MM.YYYY

Similar to table 1.12.1, tables for the target and the safety populations will be constructed:

Table 1.12.5 Prior Medications for CHC
Table 1.12.6 Prior Medications for CHC

Similar to tables 1.12.X, tables for the concurrent medications for CHC will be constructed:

for the core population

Table 1.13.1 Concurrent Medications for CHC
Table 1.13.2 Concurrent Medications for CHC (prior treatment groups)
Table 1.13.3 Concurrent Medications for CHC (treatment-experienced groups)
Table 1.13.4 Concurrent Medications for CHC (Child Pugh score groups)

for the target and safety populations

Table 1.13.5 Concurrent Medications for CHC
Table 1.13.6 Concurrent Medications for CHC

Effectiveness Analyses (TP)

AbbVie Ltd
P16-253
Table 2.1.1.1 Percentage for effectiveness endpoints
The target population (TP)
Page X of X

Parameter Statistics	Total (N=XX) n (%) [95% CI]
SVR12 achieving (single last HCV RNA value <50 IU/mL 12 weeks after the last actual dose of the ABBVIE REGIMEN)	XX (XX.X) [XX.XX - XX.XX]
SVR12 non-response	XX (XX.X) [XX.XX - XX.XX]
Patients with breakthrough (at least one documented HCV RNA value <50 IU/mL followed by HCV RNA ≧50 IU/mL during treatment)	XX (XX.X) [XX.XX - XX.XX]
Failure to suppress (each measured on-treatment HCV RNA value ≧50 IU/mL)	XX (XX.X) [XX.XX - XX.XX]
Patients with relapse (HCV RNA value <50 IU/mL at EoT or at the last on-treatment HCV RNA measurement followed by HCV RNA ≧50 IU/mL post-treatment)	XX (XX.X) [XX.XX - XX.XX]
Patients with premature study drug discontinuation with no on-treatment virological failure (breakthrough or failure to suppress)	XX (XX.X) [XX.XX - XX.XX]
Patients with missing SVR12 data	XX (XX.X) [XX.XX - XX.XX]
Patients with virological response (HCV RNA <50 IU/mL) at EoT	XX (XX.X) [XX.XX - XX.XX]

N: the number of subjects in the target population. n: number of subjects within a specific category. Percentages are calculated as 100 x (n/N).
EoT: end of treatment. SVR12: sustained virological response at 12 weeks after EoT. 95% CI: 95% confidence interval (the Clopper-Pearson method).

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie Ltd
P16-253
Table 2.1.2.1 Percentage for effectiveness endpoints without patients with missing SVR12 results
The target population (TP)
Page X of X

Parameter Statistics	Total (N=XX) n (%) [95% CI]
SVR12 achieving (single last HCV RNA value <50 IU/mL 12 weeks after the last actual dose of the ABBVIE REGIMEN)	XX (XX.X) [XX.XX - XX.XX]
SVR12 non-response	XX (XX.X) [XX.XX - XX.XX]
Patients with breakthrough (at least one documented HCV RNA value <50 IU/mL followed by HCV RNA ≧50 IU/mL during treatment)	XX (XX.X) [XX.XX - XX.XX]
Failure to suppress (each measured on-treatment HCV RNA value ≧50 IU/mL)	XX (XX.X) [XX.XX - XX.XX]
Patients with relapse (HCV RNA value <50 IU/mL at EoT or at the last on-treatment HCV RNA measurement followed by HCV RNA ≧50 IU/mL post-treatment)	XX (XX.X) [XX.XX - XX.XX]
Patients with premature study drug discontinuation with no on-treatment virological failure (breakthrough or failure to suppress)	XX (XX.X) [XX.XX - XX.XX]
Patients with virological response (HCV RNA <50 IU/mL) at EoT	XX (XX.X) [XX.XX - XX.XX]

N: the number of subjects in the target population. n: number of subjects within a specific category. Percentages are calculated as 100 x (n/N).
EoT: end of treatment. SVR12: sustained virological response at 12 weeks after end of treatment. CI^ confidence interval.
95% confidence intervals calculated using the Clopper-Pearson method.

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P15-743 (HCV RWE)
Table 2.1.X.1 SVR12 achieving. Univariate logistic regression results
The core population
Page X of X

	Total
Predictor 1	
Patients for analysis (n)	XXX
Convergence criterion status	xxxxxxxxxxxx
OR (95% Wald CI)	X.XXX (X.XXX - X.XXX)
p-value	0.XXXX
Predictor 2	
Patients for analysis (n)	XXX
Convergence criterion status	xxxxxxxxxxxx
Reference level	xxxxxxxxxxxx
OR (95% Wald CI) for Level X	X.XXX (X.XXX - X.XXX)
p-value for Male	0.XXXX
...	

SVR12: sustained virological response at 12 weeks after end of treatment. OR: odds ratio. CI: confidence interval.

Program code, date, time Data extracted: DD.MM.YYYY

AbbVie LLC
P15-743 (HCV RWE)
Table 2.1.X.2 SVR12 achieving. Multiple logistic regression results
The core population
Page X of X

	Overall
Patients for analysis (n)	XXX
Predictor 1	
OR (95% Wald CI)	X.XXX (X.XXX - X.XXX)
p-value	0.XXXX
...	

SVR12: sustained virological response at 12 weeks after end of treatment. OR: odds ratio. CI: confidence interval.

Program code, date, time Data extracted: DD.MM.YYYY

Similar to table for SVR12 achieving univariate logistic regression results, tables for the following variables (outcomes) will be constructed (if applicable):

Table 2.1.X.1 Virological response at EoT. Univariate logistic regressions results
Table 2.1.X.2 Virological response at EoT. Multiple logistic regression results

Table 2.1.X.1 Relapse after EoT. Univariate logistic regressions results
Table 2.1.X.2 Relapse after EoT. Multiple logistic regression results

Effectiveness Analyses (CP)

Similar to tables 2.1.1.X-2.1.2.X, the following tables will be constructed for the core population:

Table 2.2.1.1 Percentage for effectiveness endpoints
Table 2.2.2.1 Percentage for effectiveness endpoints without patients with missing SVR12 results

Similar to tables 2.1.X.1-2.1.X.2, tables for the following variables (outcomes) will be constructed (if applicable) for the core population:

Table 2.2.X.1 SVR12 achieving. Univariate logistic regression results
Table 2.2.X.2 SVR12 achieving. Multiple logistic regression results

Table 2.2.X.1 Virological response at EoT. Univariate logistic regressions results
Table 2.2.X.2 Virological response at EoT. Multiple logistic regression results

Table 2.2.X.1 Relapse after EoT. Univariate logistic regressions results
Table 2.2.X.2 Relapse after EoT. Multiple logistic regression results

Effectiveness Analyses (CPSFU)

Similar to tables 2.1.1.X-2.1.2.X, the following tables will be constructed for the core population with sufficient follow-up data (CPSFU):

Table 2.3.1.1 Percentage for effectiveness endpoints (main analysis)
Table 2.3.2.1 Percentage for effectiveness endpoints without patients with missing SVR12 results (main analysis)

Similar to tables 2.1.X.1-2.1.X.2, tables for the following variables (outcomes) will be constructed (if applicable) for the core population:

Table 2.3.X.1 SVR12 achieving. Univariate logistic regression results
Table 2.3.X.2 SVR12 achieving. Multiple logistic regression results

Table 2.3.X.1 Virological response at EoT. Univariate logistic regressions results
Table 2.3.X.2 Virological response at EoT. Multiple logistic regression results

Table 2.3.X.1 Relapse after EoT. Univariate logistic regressions results
Table 2.3.X.2 Relapse after EoT. Multiple logistic regression results

Exposure

AbbVie LLC
P16-253 (CITRIN)
Table 3.1 AbbVie REGIMEN intake
The safety population
Page X of X

	Total (N = XX)
Actual duration ABBVIE REGIMEN [1]	
n	XX
Mean	XX.X
SD	XX.XX
Median	XX.X
IQR	XX.X
Min	XX
Max	XX
Subjects with collected deviating duration reasons	XX (XX.X)
Reasons for deviating duration:	
AE or SAE (Physician decision)	XX (XX.X)
Virological non-response (Physician decision)	XX (XX.X)
Rebound or breakthrough (Physician decision)	XX (XX.X)
Resistance to DAA (Physician decision)	XX (XX.X)
Patient refused to continue treatment	XX (XX.X)
Patient withdrew consent to participate in the study	XX (XX.X)
Lost to follow-up	XX (XX.X)
...	...
PARITAPREVIR/R-OMBITASVIR	
Subjects with intake missing for at least 7 days in a row	XX (XX.X)
Percentage of target dose taken (%)	
Weeks 1-4	
n	XX
Mean	XX.X
SD	XX.XX
Median	XX.X
IQR	XX.X
Min	XX
Max	XX
Weeks 5-8	
n	XX
Mean	XX.X

SD	XX.XX
Median	XX.X
IQR	XX.X
Min	XX
Max	XX
Weeks 9-12	
n	XX
Mean	XX.X
SD	XX.XX
Median	XX.X
IQR	XX.X
Min	XX
Max	XX
DASABUVIR	
Subjects with intake missing for at least 7 days in a row	XX (XX.X)
Percentage of target dose taken (%)	
Weeks 1-4	
n	XX
Mean	XX.X
SD	XX.XX
Median	XX.X
IQR	XX.X
Min	XX
Max	XX
Weeks 5-8	
n	XX
Mean	XX.X
SD	XX.XX
Median	XX.X
IQR	XX.X
Min	XX
Max	XX
Weeks 9-12	
n	XX
Mean	XX.X
SD	XX.XX
Median	XX.X
IQR	XX.X
Min	XX
Max	XX

N: the number of subjects in the target population.
n: the number of subjects within a specific category. Percentages were calculated as (100 x n/N).
[1] This parameter is calculated as interval (in days) between date of first intake and date of last intake of treatment.

Adverse events

AbbVie LLC
P16-253 (CITRIN)
Table 3.2.1 Adverse events
The safety population
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System organ class (SOC) Preferred term (PT)	Total (N=XX) n (%) /E
Total [1]	XX(XX.X) /XX
System organ class 1	XX(XX.X) /XX
Preferred term A	XX(XX.X) /XX
Preferred term B	...
...	...
System organ class 2	...
...	...
...	...

N: the number of patients in the safety population.
n: the number of patients who have AE with appropriate SOC/PT. Percentages are calculated as (100 x n/N).
E: the number of AE episodes, which have an appropriate SOC and/or PT.
Patients with several AEs having the same SOC and PT are accounted only once for appropriate SOC and PT.
[1] The Total line displays the number (n) and the proportion (%) of patients who have at least on AE as well as the total number of AE episodes in the study.
The coding is carried out by the dictionary MedDRA v.20.0.
The table does not include AEs that occurred prior to the first intake of the study drug.
The data is sorted alphabetically: first by SOC, then by PT.

Program code, date, time Data extracted: DD.MM.YYYY

Similar to table 3.2.1, table 3.2.2 will be constructed:

Table 3.2.2 Serious adverse events

AbbVie LLC

P16-253 (CITRIN)

Table 3.2.3 Adverse events by relationship to the study drug

The safety population

Page X of X

System Organ Class (SOC) Preferred term (PT)	Relationship to the study drug	Total (N=XX) n (%) /E
Total [1]	Reasonable possibility	XX(XX.X) /XX
	No reasonable possibility	XX(XX.X) /XX
	Total	XX(XX.X) /XX
System Organ Class 1	Reasonable possibility	XX(XX.X) /XX
	No reasonable possibility	XX(XX.X) /XX
	Total	XX(XX.X) /XX
Preferred term A	Reasonable possibility	XX(XX.X) /XX
	No reasonable possibility	XX(XX.X) /XX
	Total	XX(XX.X) /XX
Preferred term Б	Reasonable possibility	XX(XX.X) /XX
...	...	...
System Organ Class 2	Reasonable possibility	XX(XX.X) /XX
...	...	...

N: the number of patients in the safety population.
n: the number of patients who have AE with appropriate SOC/PT. Percentages are calculated as (100 x n/N).
E: the number of AE episodes, which have an appropriate SOC and/or PT.
Each SOC/PT category includes only AEs with the highest relationship to the study drug in each patient. Each patient is counted only once in the Total lines and in the lines for each SOC or SOC/PT categories. Thus, if patient has several AEs with the same SOC and PT but different relationship to the drug, only the AEs with maximum relashionship will be accounted, while each patient will be accounted only once in line which corresponds the highest relationship of his AEs.
[1] The Total lines displays the number (n) and the proportion (%) of patients who have AEs. Each patient is counted once in line which corresponds the highest relationship of all his AEs. #E displays the number of all AEs episodes with appropriate relationship to the drug in the study.
The coding is carried out by the dictionary MedDRA v.20.0. The table does not include AEs that occurred prior to the first intake of the study drug.
The data is sorted alphabetically: first by SOC, then by PT and relationship to the drug.

Program code, date, time Data extracted: DD.MM.YYYY

Similar to table 3.2.3, table 3.2.4 will be constructed:

Table 3.2.4 Serious adverse events by relationship to the study drug

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P16-253 (CITRIN)

Table 3.2.5 Adverse events by severity

The safety population

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System Organ Class (SOC) Preferred term (PT)	Severity	Total (N=XX) n (%) /E
Total [1]	Severe	XX(XX.X) /XX
	Moderate	XX(XX.X) /XX
	Mild	
	Total	XX(XX.X) /XX
System Organ Class 1	Severe	XX(XX.X) /XX
	Moderate	XX(XX.X) /XX
	Mild	
	Total	XX(XX.X) /XX
Preferred term A	Severe	XX(XX.X) /XX
	Moderate	XX(XX.X) /XX
	Mild	
	Total	XX(XX.X) /XX
Preferred term Б	Severe	XX(XX.X) /XX
	Moderate	XX(XX.X) /XX
	Mild	
	Total	XX(XX.X) /XX
...	...	...
System Organ Class 2	Severe	XX(XX.X) /XX
	Moderate	XX(XX.X) /XX

System Organ Class (SOC) Preferred term (PT)	Severity	Total (N=XX) n (%) /E
	Mild	
	Total	XX(XX.X) /XX
...	...	...
...	...	...

N: the number of patients in the safety population.
n: the number of patients who have AE with appropriate SOC/PT. Percentages are calculated as (100 x n/N).
E: the number of AE episodes, which have an appropriate SOC and/or PT.
Each SOC/PT category includes only AEs with the highest severity in each patient. Each patient is counted only once in the Total lines and in the lines for each SOC or SOC/PT categories. Thus, if patient has several AEs with the same SOC and PT but different severity, only the AEs with maximum severity will be accounted, while each patient will be accounted only once in line which corresponds the highest severity of his AEs.
[1] The Total lines displays the number (n) and the proportion (%) of patients who have AEs. Each patient is counted once in line which corresponds the highest severity of all his AEs. #E displays the number of all AEs episodes with appropriate severity in the study.
The coding is carried out by the dictionary MedDRA v.20.0.
The table does not include AEs that occurred prior to the first intake of the study drug.
The data is sorted alphabetically: first by SOC, then by PT and relationship to the drug.

Program code, date, time

Data extracted: DD.MM.YYYY

Similar to table 3.2.5, table 3.2.6 will be constructed:

Table 3.2.6 Serious adverse events by severity

Hematology

AbbVie LLC
P16-253 (CITRIN)
Table 3.3.1 Hematology. Descriptive statistics
The safety population
Page X of X

Parameter Visit Statistics	Total (N = XX)	Change from baseline (N = XX)
Hemoglobin (unit measure)		
Visit 1		
n	XX	
Mean	XX.X	
SD	XX.XX	
Median	XX.X	
IQR	XX.X	
Min	XX	
Max	XX	
EoT		
n	XX	XX
Mean	XX.X	XX.X
SD	XX.XX	XX.XX
Median	XX.X	XX.X
IQR	XX.X	XX.X
Min	XX	XX
Max	XX	XX
SVR12		
n	XX	XX
Mean	XX.X	XX.X
SD	XX.XX	XX.XX
Median	XX.X	XX.X
IQR	XX.X	XX.X
Min	XX	XX

Parameter Visit Statistics	Total (N = XX)	Change from baseline (N = XX)
Max	XX	XX
Platelets (unit measure)		
...		
Prothrombin time (unit measure)		
...		

N: the number of patients in the safety population.
n: the number of valid measurements.
SD: standard deviation.
IQR: interquartile range.
EoT: end of treatment.
SVR12: sustained virological response at 12 weeks after end of treatment.
Table displays descriptive statistics for general blood test parameters values and their changes from baseline (visit 1).

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-253 (CITRIN)
Table 3.3.2 Hematology. Clinical assessments
The safety population
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Parameter Visit Value	Total (N = XX)
Hemoglobin	
Visit 1	
n	XXX
Normal	XX(XX.X)
Abnormal NCS	XX(XX.X)
Abnormal CS	XX(XX.X)
EoT	
n	XXX
Normal	XX(XX.X)
Abnormal NCS	XX(XX.X)
Abnormal CS	XX(XX.X)
SVR12	
n	XXX
Normal	XX(XX.X)
Abnormal NCS	XX(XX.X)
Abnormal CS	XX(XX.X)

Parameter Visit Value	Total (N = XX)
Platelets	
...	
Prothrombin time	
...	

N: the number of patients in the safety population.
n: the number of valid measurements. Percentages are based on the number of valid measurements at analyzed visit.
CS: clinically significant.
NCS: not clinically significant.
EoT: end of treatment.
SVR12: sustained virological response at 12 weeks after end of treatment.

Program code, date, time

Data extracted: DD.MM.YYYY

AbbVie LLC
P16-743 (CITRIN)
Table 3.3.3 Hematology. Shift table
The safety population
Page X of X

Parameter / Visit / Value	Baseline (visit 1) Normal	Abnormal NCS	Abnormal CS	Total assessed
Hemoglobin				
Visit 1				
Normal				XX (XX.X)
Abnormal NCS				XX (XX.X)
Abnormal CS				XX (XX.X)
Total assessed				XX (100)
EoT				
Normal	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Abnormal NCS	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Abnormal CS	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Total assessed	XX (100)	XX (100)	XX (100)	XX (100)
SVR12				
Normal	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Abnormal NCS	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Abnormal CS	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Total assessed	XX (100)	XX (100)	XX (100)	XX (100)
Platelets				

Parameter / Visit / Value	Baseline (visit 1) Normal	Baseline (visit 1) Abnormal NCS	Baseline (visit 1) Abnormal CS	Baseline (visit 1) Total assessed
...				
Prothrombin time				
...	...	...	...	...

CS: clinically significant.
NCS: not clinically significant.
EoT: end of treatment.
SVR12: sustained virological response at 12 weeks after end of treatment.
Percentages are based on the number of patients with a non-missing assessment on time point and on baseline (visit 1).

Program code, date, time Data extracted: DD.MM.YYYY

Blood chemistry

Similar to tables 3.3.1-3.3.3, the following tables will be constructed:

Table 3.4.1 Blood chemistry. Descriptive statistics
Table 3.4.2 Blood chemistry. Clinical assessments
Table 3.4.3 Blood chemistry. Shift table