# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 205834Orig1s007, s008, s009

# STATISTICAL REVIEW(S)

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Translational Sciences
Office of Biostatistics

# STATISTICAL REVIEW AND EVALUATION

## CLINICAL STUDIES

| | |
|---|---|
| **NDA/BLA Serial Number:** | 205,834 / S-0007, S-0008, and S-0009 |
| **Drug Name:** | Harvoni (ledipasvir/sofosbuvir [LDV/SOF]) tablets |
| **Indication(s):** | The treatment of Chronic Hepatitis C Infection in Adults |
| **Applicant:** | Gilead Sciences |
| **Date(s):** | Submitted: August 26, 2015<br>Received: September 02, 2015<br>PDUFA Date: February 26, 2016<br>Draft Review Completed: February 2, 2016<br>Final Review Completed: February 8, 2016 |
| **Review Priority** | Priority |
| **Biometrics Division:** | Division of Biometrics IV |
| **Statistical Reviewer:** | Wen Zeng, Ph.D. |
| **Concurring Reviewers:** | Thamban Valappil, Ph.D. Acting Statistics Team Leader |
| **Medical Division:** | Division of Antiviral Drug Products |
| **Clinical Team:** | Charu Mullick, MD; Medical Reviewer<br>Poonam Mishra, MD; Medical Team Leader |
| **Project Manager:** | Christian Yoder, MPH. Regulatory Project Manager |

**Keywords:** HCV Infected Subjects, Harvoni (LDV/SOF), Decompensated Cirrhosis, Pre- and Post-liver Transplant, Genotype 1 HCV, Genotype 4 HCV.

# Table of Contents

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES** ..... **1**

**FOOD AND DRUG ADMINISTRATION** ..... **1**

**STATISTICAL REVIEW AND EVALUATION** ..... **1**

**LIST OF TABLES** ..... **3**

**LIST OF FIGURES** ..... **6**

**1. EXECUTIVE SUMMARY** ..... **7**

**2. INTRODUCTION** ..... **9**

2.1 OVERVIEW ..... 9
*2.1.1 Study Reviewed* ..... *9*
2.2 DATA SOURCES ..... 10

**3. STATISTICAL EVALUATION** ..... **11**

3.1 DATA AND ANALYSIS QUALITY ..... 11
3.2 EVALUATION OF EFFICACY ..... 11
*3.2.1 Study Design and Endpoints* ..... *11*
*3.2.2 SOLAR-1 (GS-US-337-0123)* ..... *15*
*3.2.3 SOLAR-2 (GS-US-337-0124)* ..... *20*
*3.2.4 Combination of SOLAR-1 and SOLAR-2* ..... *25*
3.3 EVALUATION OF SAFETY ..... 31

**4. FINDINGS IN SPECIAL/SUBGROUP POPULATIONS** ..... **31**

4.1 BASELINE CIRRHOSIS STATUS AND GENOTYPES ..... 32
4.2 GENDER, RACE, AGE, AND GEOGRAPHIC REGION ..... 34
4.3 OTHER SPECIAL/SUBGROUP POPULATIONS ..... 34

**5. SUMMARY AND CONCLUSIONS** ..... **35**

5.1 STATISTICAL ISSUES AND COLLECTIVE EVIDENCE ..... 35
5.2 CONCLUSIONS AND RECOMMENDATIONS ..... 35
5.3 LABELING RECOMMENDATIONS ..... 36

**REFERENCES** ..... **116**



Reference ID: 3884456

**LIST OF TABLES**

**Table 1** List of Phase 2 studies included in this review ..... 10
**Table 2** On-Treatment Analysis (Visit) Windows for Phase 2 Studies ..... 15
**Table 3** Post-treatment and Post-transplantation Analysis (Visit) Windows for Phase 2 Studies ..... 15
**Table 4:** Subjects Disposition for Study SOLAR-1 (FAS) ..... 16
**Table 5:** Applicant's Results of SVR12 for Study SOLAR-1 (FAS) ..... 17
**Table 6:** The Summary of Changes of 20 Subjects who had Different Planned and Actual Treatment Group for Study SOLAR-1 (FAS) ..... 18
**Table 7:** The Subjects' Baseline CPT Category and Their Actual Group Assignment for Study SOLAR-1 (FAS) ..... 19
**Table 8:** Primary Efficacy Results (SVR12) by Group for SOLAR-1 (Efficacy Analysis Set) ..... 20
**Table 9:** SVR12 Rate by Group Combination (Pre vs. Post) for SOLAR-1 (Efficacy Analysis Set) ..... 20
**Table 10:** SVR12 Rate by Group Combination (CPT Category) for SOLAR-1 (Efficacy Analysis Set) ..... 20
**Table 11:** Subjects Disposition for Study SOLAR-2 (FAS) ..... 21
**Table 12:** Applicant's Results of SVR12 for Study SOLAR-1 (FAS) ..... 22
**Table 13:** The Summary of Changes of 20 Subjects who had Different Planned and Actual Treatment Group for Study SOLAR-2 (FAS) ..... 23
**Table 14:** The Subjects' Baseline CPT Category and Their Actual Group Assignment for Study SOLAR-2 (FAS) ..... 23
**Table 15:** Primary Efficacy Results (SVR12) of GT-1 by Group for SOLAR-2 (Efficacy Analysis Set) ..... 24
**Table 16:** SVR12 Rate of GT-1 by Group Combination (Pre vs. Post) for SOLAR-2 (Efficacy Analysis Set) ..... 25
**Table 17:** SVR12 Rate of GT-1 by Group Combination (CPT Category) for SOLAR-2 (Efficacy Analysis Set) ..... 25
**Table 18:** Applicant's Results of SVR12 for Combination of SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ..... 26
**Table 19:** Primary Efficacy Results (SVR12) of GT-1 by Group for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ..... 27
**Table 20:** SVR12 Rate of GT-1 by Group Combination (Pre vs. Post) for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ..... 27
**Table 21:** SVR12 Rate of GT-1 by Group Combination (CPT Category) for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ..... 27
**Table 22:** Relapse Rates of GT-1 by Group in 12 Weeks Arm for SOLAR-1 and SOLAR-2 Combined (Efficacy Analysis Set) ..... 28
**Table 23:** Relapse Rates of GT-1 by Group in 24 Weeks Arm for SOLAR-1 and SOLAR-2 Combined (Efficacy Analysis Set) ..... 28
**Table 24**: Subgroup Analysis of SVR12 of GT-1 Subjects for Combination of SOLAR-1 and SOLAR-2 in Group 3 and Group 4 (Efficacy Analysis Set) ..... 32

**Table 25**: Subgroup Analysis of SVR12 of GT-1 Subjects for Combination of SOLAR-1 and SOLAR-2 in Group 1, Group2, Group 5 and Group 6 (Efficacy Analysis Set) ..... 33
**Table 26:** Primary Efficacy Results (SVR12) of GT-1 by Group for SOLAR-1 and SOLAR-2 without 12 Principal Investigators Data (Efficacy Analysis Set) ..... 35
**Table 27:** Demographics and Baseline Characteristics for Study SOLAR-1 (FAS) ..... 37
**Table 28:** Demographics and Baseline Characteristics of Group 1 in Study SOLAR-1 (FAS) ..... 39
**Table 29:** Demographics and Baseline Characteristics of Group 2 in Study SOLAR-1 (FAS) ..... 41
**Table 30:** Demographics and Baseline Characteristics of Group 3 in Study SOLAR-1 (FAS) ..... 44
**Table 31:** Demographics and Baseline Characteristics of Group 4 in Study SOLAR-1 (FAS) ..... 46
**Table 32:** Demographics and Baseline Characteristics of Group 5 in Study SOLAR-1 (FAS) ..... 48
**Table 33:** Demographics and Baseline Characteristics of Group 6 in Study SOLAR-1 (FAS) ..... 51
**Table 34:** Demographics and Baseline Characteristics of Group 7 in Study SOLAR-1 (FAS) ..... 53
**Table 35:** The List of Subjects who had Different Planned and Actual Treatment Group for Study SOLAR-1 (FAS) ..... 56
**Table 36:** The List of Subjects who had Liver Transplant during the Study for SOLAR-1 (FAS) ..... 56
**Table 37:** Demographics and Baseline Characteristics of for Study SOLAR-2 (Safety) ..... 57
**Table 38:** Demographics and Baseline Characteristics of Group 1 in Study SOLAR-2 (Safety) ..... 59
**Table 39:** Demographics and Baseline Characteristics of Group 2 in Study SOLAR-2 (Safety) ..... 62
**Table 40:** Demographics and Baseline Characteristics of Group 3 in Study SOLAR-2 (Safety) ..... 65
**Table 41:** Demographics and Baseline Characteristics of Group 4 in Study SOLAR-2 (Safety) ..... 67
**Table 42:** Demographics and Baseline Characteristics of Group 5 in Study SOLAR-2 (Safety) ..... 70
**Table 43:** Demographics and Baseline Characteristics of Group 6 in Study SOLAR-2 (Safety) ..... 73
**Table 44:** Demographics and Baseline Characteristics of Group 7 in Study SOLAR-2 (Safety) ..... 75
**Table 45:** The List of Subjects who had Different Planned and Actual Treatment Group for Study SOLAR-2 (FAS) ..... 77
**Table 46:** The List of Subjects who had Liver Transplant during the Study for SOLAR-2 (FAS) ..... 78
**Table 47:** Primary Efficacy Results (SVR12) by Group for SOLAR-2 (Efficacy Analysis Set) ..... 78



Reference ID: 3884456

**Table 48:** SVR12 Rate of by Group Combination (Pre vs. Post) for SOLAR-2 (Efficacy Analysis Set) ....78
**Table 49:** SVR12 Rate of by Group Combination (CPT Category) for SOLAR-2 (Efficacy Analysis Set) ....78
**Table 50:** Demographics and Baseline Characteristics of Studies SOLAR-1 and SOLAR-2 (Safety) ....79
**Table 51:** Demographics and Baseline Characteristics of Group 1 in Studies SOLAR-1 and SOLAR-2 (Safety) ....81
**Table 52:** Demographics and Baseline Characteristics of Group 2 in Studies SOLAR-1 and SOLAR-2 (Safety) ....84
**Table 53:** Demographics and Baseline Characteristics of Group 3 in Studies SOLAR-1 and SOLAR-2 (Safety) ....87
**Table 54:** Demographics and Baseline Characteristics of Group 4 in Studies SOLAR-1 and SOLAR-2 (Safety) ....89
**Table 55:** Demographics and Baseline Characteristics of Group 5 in Studies SOLAR-1 and SOLAR-2 (Safety) ....92
**Table 56:** Demographics and Baseline Characteristics of Group 6 in Studies SOLAR-1 and SOLAR-2 (Safety) ....94
**Table 57:** Demographics and Baseline Characteristics of Group 7 in Studies SOLAR-1 and SOLAR-2 (Safety) ....97
**Table 58:** Primary Efficacy Results (SVR12) by Group for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ....99
**Table 59:** SVR12 Rate by Group Combination (Pre vs. Post) for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ....99
**Table 60:** SVR12 Rate by Group Combination (CPT Category) for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ....99
**Table 61:** The MELD Score Changes at FU-12 Weeks from Baseline for Subjects who Received 12 Weeks Treatment and Had SVR12=Success in Groups 1, 2, 5, and 6 of SOLAR-1 and SOLAR-2 Combined. ....100
**Table 62:** The MELD Score Changes at FU-12 Weeks from Baseline for Subjects who Received 12 Weeks Treatment and Had SVR12=Failure in Groups 1, 2, 5, and 6 of SOLAR-1 and SOLAR-2 Combined. ....100
**Table 63:** The CPT Category Changes at FU-12 Weeks from Baseline for Subjects who Received 12 Weeks Treatment in Groups 1, 2, 5, and 6 of SOLAR-1 and SOLAR-2 Combined. ....101
**Table 64:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 1 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ....101
**Table 65:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 2 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ....103
**Table 66:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 3 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ....104
**Table 67:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 4 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ....106
**Table 68:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 5 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ....107



Reference ID: 3884456

**Table 69:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 6 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ..... 109
**Table 70:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 7 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ..... 111
**Table 71:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In the combination of Group 1, 2, 5 and 6 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ..... 112
**Table 72:** Primary Efficacy Results (SVR12) of GT-4 by Group for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ..... 114
**Table 73:** Subgroup Analyses of SVR12 of GT-4 Subjects Only of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set) ..... 114
**Table 74:** SVR12 Rate of GT-1 by Group Combination (Pre vs. Post) for SOLAR-1 and SOLAR-2 without 12 Principal Investigators Data (Efficacy Analysis Set) ..... 115
**Table 75:** SVR12 Rate of GT-1 by Group Combination (CPT Category) for SOLAR-1 and SOLAR-2 without 12 Principal Investigators Data (Efficacy Analysis Set) ..... 115

## LIST OF FIGURES

**Figure 1**: Study Diagram of SOLAR-1 and SOLAR-2 ..... 12
Figure 2: The MELD Score Changes at FU-12 from Baseline for Subjects who Had SVR12=Success in Decompensated Groups (Groups 1, 2, 5 and 6) in the Combination of SOLAR-1 and SOLAR-2 (Baseline MELD score<15). ..... 29
Figure 3: The MELD Score Changes at FU-12 from Baseline for Subjects who Had SVR12=Success in Decompensated Groups (Groups 1, 2 , 5 and 6) in the Combination of SOLAR-1 and SOLAR-2 (Baseline MELD score⩾15) ..... 30
Figure 4: The MELD Score Changes at FU-12 Weeks from Baseline for Subjects who Had SVR12=Success in Groups 1, 2, 5, and 6 of SOLAR-1 and SOLAR-2 Combined (A: subjects had MELD<15 at baseline; B: subjects had MELD⩾15 at baseline) ..... 31
Figure 5: The MELD Score Changes at FU-24 Weeks from Baseline for Subjects who Had SVR12=Success in Groups 1, 2, 5, and 6 of SOLAR-1 and SOLAR-2 Combined (A: subjects had MELD<15 at baseline; B: subjects had MELD⩾15 at baseline) ..... 31



Reference ID: 3884456

# 1. EXECUTIVE SUMMARY

Harvoni® (ledipasvir/sofosbuvir [LDV/SOF]) is an all oral, once daily, fixed-dose combination of LDV and SOF. LDV/SOF was first approved for commercial marketing in the United States on 10 October 2014 for the treatment of treatment-naïve and treatment-experienced patients mono-infected with genotype (GT) 1 hepatitis C virus (HCV), with and without compensated cirrhosis. On November 2015, Harvoni was approved for patients with HCV/HIV-1 co-infection, patients with chronic genotype 4, 5, or 6 HCV infection, and treatment experienced patients with cirrhosis.

This efficacy supplement proposes to extend the indication to support the use of Harvoni plus ribavirin (RBV) 12 weeks for the treatment of patients with decompensated liver disease due to chronic hepatitis C (CHC) infection and patients with hepatitis C recurrence after liver transplantation. Two phase 2 studies, GS-US-337-0123 (SOLAR-1) and GS-US-337-0124 (SOLAR-2) are provided in support of the proposed extension to the indication.

SOLAR-1 and SOLAR-2 have identical study designs: multicenter, open-label studies in genotype 1 and 4 HCV-infected adults who have advanced liver disease or are post-liver transplant. Subjects were randomized in a 1:1 ratio to receive 12 or 24 weeks of LDV/SOF (given once daily) + RBV (given as a divided dose twice daily) within each of 7 groups characterized by liver transplantation status and severity of hepatic impairment as follows:

**Group 1:** pre-transplant subjects with decompensated cirrhosis as measured by the Child-Pugh-Turcotte score B (CPT B) at baseline
**Group 2:** pre-transplant subjects with decompensated cirrhosis as measured by the CPT C
**Group 3:** post-transplant subjects without cirrhosis and no evidence of hepatic decompensation (F0-F3 Fibrosis)
**Group 4:** post-transplant subjects with compensated cirrhosis as measured by the CPT A,
**Group 5:** post-transplant subjects with decompensated cirrhosis as measured by the CPT B
**Group 6:** post-transplant subjects with decompensated cirrhosis as measured by the CPT C and
**Group 7:** post-transplant subjects with fibrosing cholestatic hepatitis (FCH)

Group 3 was to randomize up to 100 subjects, and all other groups were to randomize up to 50 subjects. Subjects with CPT score >12 were excluded from the studies. The only difference between the two studies was that SOLAR-1 was conducted in the United States, and SOLAR-2 was conducted in Europe, Canada, Australia and New Zealand. Both studies had very similar SVR12 rate results for the 12-week and 24-week treatment arms in each of 7 Groups, and the subgroup analyses by region were consistent. Thus, this review presents results from the two studies combined (Table 19) as well as results from the individual studies (Table 8 and Table 15).

A total of 670 subjects received the study drug: 337 from SOLAR-1 and 333 from SOLAR-2. Three subjects who did not have advanced liver disease in SOLAR-2 and did not qualify for Cohort A were excluded from the full analysis set. In addition, six subjects in SOLAR-1 and 7 subjects in SOLAR-2 who had liver transplants during the trials and did not have a SVR12 visit were excluded from the efficacy analyses. As a result, the final number of subjects for the



Reference ID: 3884456

efficacy analyses was 654 (329 subjects received 12 weeks of treatment and 325 subjects received 24 weeks of treatment). Out of these 654, 614 subjects (307 subjects received 12 weeks of treatment and 307 subjects received 24 weeks of treatment) had GT-1 HCV infection and 40 subjects (22 subjects received 12 weeks of treatment and 18 subjects received 24 weeks of treatment) had GT-4 HCV infection.

The SVR-12 rates for GT-1 HCV infected subjects in the 12-week treatment arm are shown in the Table 19 from the body of the review.

Table 19: SVR12 of GT-1 by Group for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Cohort | Group | T12WK* | T24WK |
|---|---|---|---|
| **A (pre-transplant)** | **G1: CPT B** | **86.5% (45/52) (74.2, 94.4)** | **92.0% (46/50) (80.8, 97.8)** |
| | G2: CPT C | 87.5% (35/40) (73.2, 95.8) | 82.6% (38/46) (68.6, 92.2) |
| B (Post-transplant) | G3: F0-F3 Fibrosis | 95.0% (94/99) (88.6, 98.3) | 99.0% (99/100) (94.6, 100.0) |
| | G4: CPT A | 98.2% (55/56) (90.5, 100.0) | 96.2% (51/53) (87.0, 99.5) |
| | **G5: CPT B** | 89.1% (41/46) (76.4, 96.4) | 95.6% (43/45) (84.9, 99.5) |
| | G6: CPT C | 57.1% (4/7) (18.4, 90.1) | 77.8% (7/9) (40.0, 97.2) |
| | G7: FCH | 100% (7/7) (59.0, 100.0) | 100% (4/4) (39.8, 100.0) |

*: SVR12 rate (n/N) and 95% confidence interval (CI). T12WK = 12 weeks of treatment; T24WK = 24 weeks of treatment; G1 – G7 denotes the seven groups.

The highest SVR12 rates were observed in Group 3 and Group 4 subjects. The SVR12 rate in the decompensated cirrhotic subjects in Groups 1 and 5 was about 87% to 89% regardless of the transplant status. The SVR12 rate in the decompensated cirrhotic subjects in Groups 2 and 6 was 88% in pre-transplant subjects and 57% in pre-transplant subjects. The sample size was limited in Group 6 and the 95% confidence intervals overlapped for the varying treatment durations.

The SVR12 rates of the 7 groups in the 24-week treatment arm were very similar to what was observed in the 12-week treatment arm. Although the combined results are presented here, results from the individual studies yielded similar findings.

For the 22 GT-4 HCV infected subjects who received 12 weeks of treatment, the SVR12 rate was 92% (11/12) for subjects without cirrhosis or with compensated cirrhosis in the post-transplant cohort. Regardless the transplant status, the SVR12 rate was 83% (5/6) for subjects with decompensated cirrhosis CPT B, and the SVR12 rate was 25% (1/4) for subjects with decompensated cirrhosis CPT C.

In conclusion, the results from the two studies demonstrated the efficacy of Harvoni plus RBV for 12 weeks in liver transplant GT-1 or GT-4 HCV infected subjects without cirrhosis or with compensated cirrhosis (CPT A), and in GT-1 HCV infected subjects with decompensated cirrhosis (CPT B or C) regardless of the transplant status. As there were no statistical "win" criteria for these studies, the finding of efficacy was primarily based on clinically acceptable SVR12 rates.

**Key statistical issues:** None.



Reference ID: 3884456

## 2. INTRODUCTION

This review evaluates an efficacy supplement from Gilead Science to determine the efficacy of Harvoni.

### 2.1 Overview

Harvoni® (ledipasvir/sofosbuvir [LDV/SOF 90/400 mg]) is an all oral, once daily, fixed-dose combination (FDC) first approved for commercial marketing in the United States (US) on 10 October 2014 for the treatment of TN and TE GT-1 hepatitis C virus (HCV), with and without compensated cirrhosis. On November 2015, Harvoni was approved for patients with HCV/HIV-1 coinfection, patients with chronic genotype 4, 5, or 6 HCV infection, and patients who are treatment-experienced and have cirrhosis at baseline.

According to the applicant, there is a medical need for treatment for patients with decompensated liver disease due to chronic hepatitis C (CHC) infection and for patients with hepatitis C recurrence after liver transplantation. In the US, over 3 million people are estimated to be chronically infected with HCV, with over 800,000 patients estimated to have cirrhosis, and more than 100,000 of these patients estimated to have decompensated cirrhosis. Unfortunately, only approximately 4500 patients with HCV out of these 100,000 patients with decompensated liver disease due to HCV are listed in a given year for transplantation, and only approximately 1500 liver transplantations for HCV are performed annually.

Patients with Child-Pugh-Turcotte (CPT) A cirrhosis (score of 5 to 6) are considered compensated. Patients with CPT B (score of 7 to 9) and CPT C (score of 10 to 15) cirrhosis are considered to have worsening degrees of decompensated cirrhosis.

In this sNDA submission, the applicant proposes the use of Harvoni with ribavirin for treatment-naive and treatment-experienced adult subjects with chronic genotype 1 or 4 HCV infection, who were post-transplantation with compensated liver disease or with decompensated liver disease, regardless of transplantation status.

- Supplement, S-007: Liver Transplant Recipients with Genotype 1 HCV Infection
- Supplement, S-008: Liver Transplant Recipients with Genotype 4 HCV Infection
- Supplement, S-009: Patients with Decompensated Cirrhosis with Genotype 1 HCV Infection

Two Phase 2 studies) included in this application support the safety and efficacy of LDV/SOF+RBV for 12 weeks in these patient populations.

#### 2.1.1 Study Reviewed

The detailed description of the studies is listed in Table 1. Two Phase 2 studies, GS-US-337-0123 (SOLAR-1) and GS-US-337-0124 (SOLAR-2), were submitted and reviewed in the efficacy supplement. Two studies have identical study design, and SOLAR-1 was in the US only while SOLAR-2 was in Europe, Canada, Australia, and New Zealand.



Reference ID: 3884456

**Table 1** List of Phase 2 studies included in this review

| Study | Phase and Design | Primary hypothesis | Treatment Period | # of Subjects per Arm | Study Population |
|---|---|---|---|---|---|
| GS-US-337-0123 (SOLAR-1)<br><br>In US | Phase 2, randomized, open-label, multicenter study<br>Genotype 1 and 4;<br><br>Subjects were enrolled into two cohorts of 7 groups. Within each group, subjects were randomized 1:1 to receive LDV/SOF+RBV for 12 or 24 weeks.<br><br>**Cohort A:**<br>Subjects with cirrhosis who had not received a liver transplantation were enrolled into 1 of 2 groups based on severity of hepatic impairment.<br>- Group 1: CPT B<br>- Group 2: CPT C<br><br>**Cohort B:**<br>Post-transplantation subjects with or without cirrhosis were enrolled into 5 groups based on severity of hepatic impairment.<br>- Group 3: Fibrosis State F0-F3<br>- Group 4: CPT A<br>- Group 5: CPT B<br>- Group 6: CPT C<br>- Group 7: FCH | There was no formal hypothesis in the protocol.<br><br>The primary objective was to explore the antiviral efficacy of combination therapy with SOF/LDV FDC + RBV for 12 or 24 weeks in subjects with advanced liver disease (either pre-liver transplant or not currently wait-listed) and post-liver transplant HCV subjects with cirrhosis as measured by SVR 12 weeks after discontinuation of therapy (SVR12 defined as HCV RNA< Lower Limit of Quantification [LLOQ] 12 weeks post-treatment) | LDV/SOF+ RBV for 12 or 24 weeks | 339 randomized and 337 dosed.<br><br>All of 337 have HCV-1, except 5 subjects with HCV-4. | Treatment-naive and treatment-experienced adult subjects with chronic genotype 1 or 4 HCV infection, who were post-transplantation with compensated liver disease or with decompensated liver disease, regardless of transplantation status |
| GS-US-337-0124 (SOLAR-2)<br><br>In Europe, Canada, Australia, New Zealand | | | | A total of 334 subjects were randomized in the study. Of the randomized subjects, 333 received at least 1 dose of study drug and were included in the Safety Analysis Set. One subject (Subject 6437-76702) was randomized but died prior to receiving any treatment.<br><br>Out of these 333, 3 subjects did not have advanced liver disease and excluded from FAS analysis. | |

The detailed design characteristics of the two phase 2 studies are described in section 3.2.1.

### 2.2 Data Sources

This efficacy supplement contains the efficacy, safety, and some genotyping results for subjects in SOLAR-1 and SOLAR-2,. The following tasks were done as part of the review process:

1. Reviewed protocols, statistical analysis plans, efficacy results and conclusions in the following submitted documents entitled "Statistics Section":
    - Module 1- labeling materials
    - Module 2- 2.5 Clinical Overview and 2.7.3 Summary of Clinical Efficacy



Reference ID: 3884456

- Module 5- Clinical Study Reports (CSRs) of the Phase 2 Studies GS-US-337-0123 (SOLAR-1) and GS-US-337-0124 (SOLAR-2).

2. Converted SAS transport files '*.xpt' in the \analysis\adam\datasets subfolder as analysis datasets, converted some of the raw datasets in the \tabulations\sdtm subfolder into SAS datasets for verification based on the definitions in 'define.xml', 'blankcrf.pdf', and the Statistical Analysis Plan in the CSR. These files are under the CDER Electronic Document Room (EDR) directory of

   \\CDSESUB1\evsprod\NDA205834\0082\m5\datasets\gs-us-337-0123
   \\CDSESUB1\evsprod\NDA205834\0082\m5\datasets\gs-us-337-0124

# 3. STATISTICAL EVALUATION

Studies SOLAR-1 and SOLAR-2 are reviewed separately and jointly under each of following sections. All tables and figures were generated by the statistical reviewer unless otherwise cited. The 12-week treatment arm was abbreviated as "**T12WK**", and "**T24WK**" was used to represent the 24-week treatment arm in the summary tables. For both studies, the primary efficacy endpoint is **SVR12** defined as HCV RNA < LLOQ target detected (TD) or target not detected (TND) 12 weeks after end of treatment.

## 3.1 Data and Analysis Quality

Overall, the reviewer reproduced primary efficacy variables in the primary efficacy analysis dataset, ADEFF, for both studies.

## 3.2 Evaluation of Efficacy

### 3.2.1 Study Design and Endpoints

SOLAR-1 and SOLAR-2 have identical study designs and the only difference was that SOLAR-1 was conducted in the US while SOLAR-2 was conducted in Europe, Canada, Australia, and New Zealand.

SOLAR-1 and SOLAR-2 were multi-center, open-label studies in genotype 1 and 4 HCV-infected adult male and female subjects. Approximately 400 subjects were planned to be randomized into the study. Subjects were randomized in a 1:1 ratio to receive 12 or 24 weeks of LDV/SOF (given once daily) + RBV (given as a divided dose twice daily) within each group from 1 to 7 (Figure 1). Approximately 100 subjects were planned to be enrolled in Cohort A and 300 subjects in Cohort B. There were no pre-specified enrollment limits for sites. Group 3 was to randomize up to 100 subjects, and all other groups were to randomize up to 50 subjects. Subjects with CPT score >12 were excluded from the studies.



Reference ID: 3884456

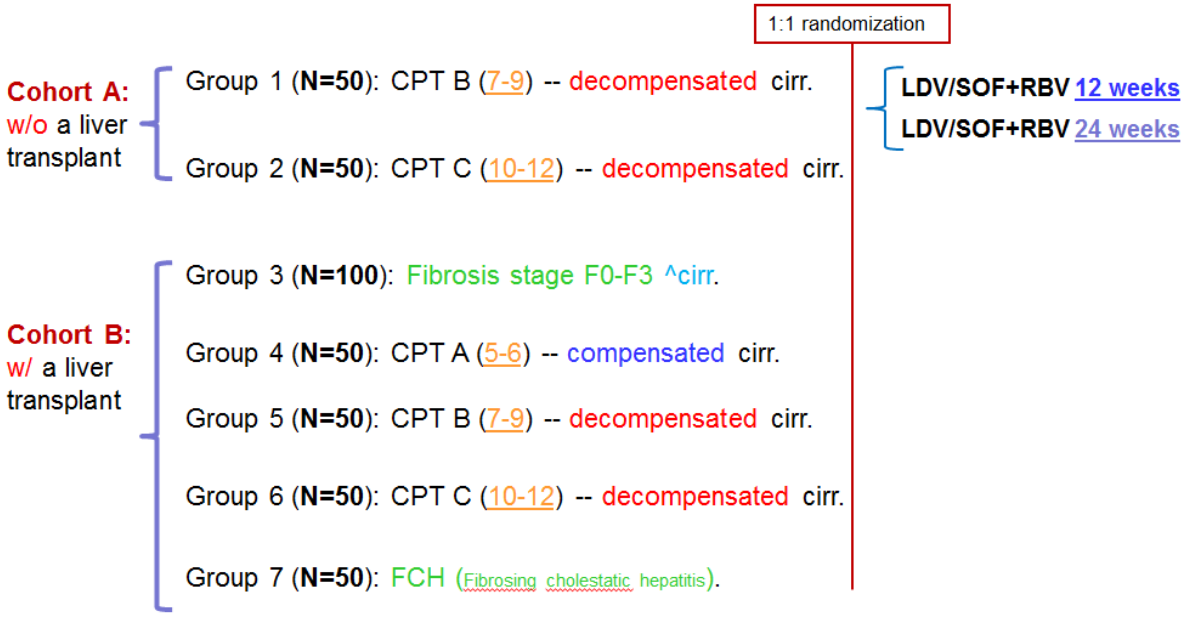


**Figure 1**: Study Diagram of SOLAR-1 and SOLAR-2

**Primary Objective:**

- To explore the antiviral efficacy of combination therapy with ledipasvir/sofosbuvir (LDV/SOF) fixed-dose combination (FDC) + ribavirin (RBV) for 12 or 24 weeks in subjects with advanced liver disease (either pre-liver transplant or not currently wait-listed) and post-liver transplant Hepatitis C virus (HCV) subjects as measured by sustained virologic response (SVR) 12 weeks after discontinuation of therapy (**SVR12**, defined as HCV RNA < lower limit of quantitation [LLOQ] 12 weeks post-treatment)

**Some Secondary Objectives:**

- To determine the proportion of subjects who attain SVR at 2, 4, 8, and 24 weeks after discontinuation of therapy (SVR2, SVR4, SVR8, and SVR24);
- To determine therapeutic efficacy as measured by the change of CPT score and the Model for End-Stage Liver Disease (MELD) score

**Primary Efficacy Endpoint:**

- **SVR12**: defined as HCV RNA < lower limit of quantitation [LLOQ] 12 weeks post-treatment.

**Secondary Efficacy Endpoints:**

- **Relapse:** HCV RNA ≥ LLOQ during the post-treatment period having achieved HCV RNA < LLOQ at the last observed on-treatment HCV RNA measurement, confirmed with consecutive values or last available post-treatment measurement.



Reference ID: 3884456

- **SVR2, SVR4, SVR8, and SVR24:** the proportion of subjects who attain SVR at 2, 4, 8, and 24 weeks after discontinuation of therapy.

**Sample Size:**

There was no formal sample size calculation.

Approximately 25 subjects per group and treatment duration (12 or 24 weeks) were planned to be enrolled with the exception of Group 3; 50 subjects per treatment duration were planned to be enrolled into the study for Group 3.

Historical SVR rates for each of the groups differ depending on the severity of disease and patient characteristics of that group. The table below provides observed SVR12 rates and the corresponding lower bound of a 1-sided 95% CI (same as the lower bound of a 2-sided 90% CI) using the Clopper-Pearson method for sample sizes of 25 and 50 subjects per treatment duration within a group.

| Observed SVR-12 Rate | 20% | 40% | 60% | 80% | 88% | 96% |
|---|---|---|---|---|---|---|
| Lower Bound 1-sided 95% CI (25 per group/duration) | 8.3% | 23.6% | 41.7% | 62.5% | 71.8% | 82.4% |
| Lower Bound 1-sided 95% CI (50 per group/duration) | 11.3% | 28.3% | 47.4% | 68.4% | 77.7% | 87.9% |

*Note: these are phase 2 studies and the winning criteria were not set up in the protocol. The efficacy assessment here is to compare the SVR12 rates from these trials to the current available treatments and to ensure the proposed regimen is clinically acceptable. As shown later, the SVR12 rates from these two studies are clinically acceptable.*

**Populations for Analyses:**

- **Safety Analysis Set (Safety):** includes all subjects who were randomized into the study and received at least 1 dose of study drug.

- **Full Analysis Set (FAS):** includes all subjects who were randomized into the study and received at least 1 dose of study drug and had genotype 1 or 4 HCV infection. The FAS was used for efficacy and safety analyses.

- **Efficacy Analysis Population:** There were some subjects who had a liver transplant during the trial before the subject reached the SVR12. Some of them were excluded from the final efficacy analyses depending on the data availability. As a result, the numbers of



Reference ID: 3884456

subjects used in the efficacy analyses varied slightly from the FAS. This will be discussed for each study separately in the efficacy result section.

Results were presented by arm (T12WK vs. T24WK) and overall for treated subjects. For binary efficacy endpoints, response rates and two-sided 95% CIs based on the normal approximation to the binomial distribution will be presented.

**How to handle multiple records within a 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. When a single value is needed, the following rule(s) will be used:

- Select the record closest to the nominal day (ie, visit weeks × 7 days) for that visit; except for post-treatment HCV RNA, MELD, and CPT visits and posttransplant HCV RNA visits, for which the latest record in the analysis window will be selected.
- If there are 2 visits equidistant from the nominal day, take the latest.
- If there is more than 1 record on the selected day, take the average (for continuous data) or the worst (for categorical data). If there are 2 values on the same day, the second may be a retest because there was a problem with the first test (for example, specimen hemolyzed). In cases where the first test is cancelled, the retest value should be used.

## Analysis Windows

***Study Day 1*** is defined as the day of the first dose of any study medication (ie, first dosing date of LDV/SOF or RBV). Study day 1 is the first non-missing chronologic start date for LDV/SOF or RBV in EX SAS dataset.

***Study Day 1 of Post-treatment follow-up*** will be the date of last dose of any study drug +1 where date of last dose of study drug is the last chronological end date on the study drug administration form of the 2 study drugs administered to the subject where the "subject permanently discontinued" flag is marked.

***Study Day 1 of Post-transplant Phase*** is defined as the date of the liver transplant on the transplant eCRF.

The general analysis windows are listed in Table 2 and 3 below.



Reference ID: 3884456

**Table 2** On-Treatment Analysis (Visit) Windows for Phase 2 Studies

| Visit ID | On-Treatment Visit Windows for HCV RNA, MELD, CPT, Safety Labs, and Vital Signs | Visit Windows for Height, Weight, and 12-Lead ECG |
|---|---|---|
| Baseline | Study Day ≤ 1 | Study Day ≤ 1 |
| Week 1 | 2 ≤ Study Day ≤ 11 | N/A |
| Week 2 | 12 ≤ Study Day ≤ 21 | N/A |
| Week 4 | 22 ≤ Study Day ≤ 35 | 2 ≤ Study Day ≤ 56* |
| Week 6 | 36 ≤ Study Day ≤ 49 | N/A |
| Week 8 | 50 ≤ Study Day ≤ 70 | N/A |
| Week 12 | 71 ≤ Study Day ≤ 98 | 57 ≤ Study Day ≤ 126 |
| Week 16# | 99 ≤ Study Day ≤ 126 | N/A |
| Week 20# | 127 ≤ Study Day ≤ 154 | N/A |
| Week 24# | 155 ≤ Study Day ≤ 182 | 127 ≤ Study Day ≤ 182 |

# Weeks 16, 20, and 24 are only applicable for subjects randomized to 24 week treatment duration.
* Height and weight are not collected at Week 4.
NOTE: Safety Labs include hematology, chemistry, urinalysis, and coagulation.

Source: the Table 1 in the SAP for the study SOLAR-1.

**Table 3** Post-treatment and Post-transplantation Analysis (Visit) Windows for Phase 2 Studies

| Posttreatment or Posttransplant FU Visit ID | Posttreatment or Posttransplant Visit Windows for HCV RNA [a] and Posttreatment Visit Windows CPT and MELD (Days from Date of Last Dose or Transplant) | Safety Laboratory Tests[b] (Days from Last Study Drug Dose) |
|---|---|---|
| FU-2 or PTx-2 | (7 HCV RNA) OR 3 (CPT and MELD) ≤ FU or PTx Day ≤ 20 | 3 ≤ FU Day ≤ 20 |
| FU-4 or PTx-4 | 21 ≤ FU or PTx Day ≤ 41 | 21 ≤ FU Day ≤ 30 |
| FU-8 or PTx-8 | 42 ≤ FU or PTx Day ≤ 69 | N/A |
| FU-12 or PTx-12 | 70 ≤ FU of PTx Day ≤ 146 | N/A |
| FU-24 or PTx-24 | 147 ≤ FU or PTx Day ≤ 190 | N/A |

a SVR or PTVR follow-up visit window (lower bound) must occur within 7 (SVR2, SVR4), 14 (SVR8, SVR12), or 21 days (SVR24) of target, respectively.
b Safety labs will only be summarized up to the 4-week follow up visit (up to 30 days post last dose). Vital signs and ECGs are only collected while subjects are on treatment. CPT and MELD scores collected posttransplant are excluded from summaries.

Source: the Table 2 in the SAP for the study SOLAR-1.

Results will be presented by each study first and followed by the combination of two studies.

### 3.2.2 SOLAR-1 (GS-US-337-0123)

#### 3.2.2.1 Patient Disposition

For SOLAR-1, a total of 339 subjects were randomized and 2 of them were not dosed and were excluded from the Safety and FAS populations. Table 4 describes the subject disposition of subjects in FAS. The majority of treated subjects (93%) completed the designed treatment period



Reference ID: 3884456

and 92% of subjects completed the designed all study visits. Twenty-five subjects (7.4%) prematurely discontinued study treatment, mainly due to adverse event (12 subjects, 3.6%).

**Table 4:** Subjects Disposition for Study SOLAR-1 (FAS)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| N | 169 | 168 | 337 |
| Completed Treatment Period | | | |
| Y | 162( 95.9%) | 150( 89.3%) | 312( 92.6%) |
| N | 7( 4.1%) | 18( 10.7%) | 25( 7.4%) |
| Reasons of NOT completed treatment | | | |
| Adverse Event | 4( 57.1%) | 8( 44.4%) | 12( 48.0%) |
| Death | 1( 14.3%) | 3( 16.7%) | 4( 16.0%) |
| Investigator's Discretion | 1( 14.3%) | .( . %) | 1( 4.0%) |
| Liver Transplant | 1( 14.3%) | 3( 16.7%) | 4( 16.0%) |
| Lost To Follow-Up | .( . %) | 1( 5.6%) | 1( 4.0%) |
| Non-Compliance With Study Drug | .( . %) | 1( 5.6%) | 1( 4.0%) |
| Protocol Violation | .( . %) | 1( 5.6%) | 1( 4.0%) |
| Withdrew Consent | .( . %) | 1( 5.6%) | 1( 4.0%) |
| Completed Study | | | |
| Y | 152( 89.9%) | 146( 93.6%) | 298( 91.7%) |
| N | 17( 10.1%) | 10( 6.4%) | 27( 8.3%) |
| Reasons of NOT completed study | | | |
| Adverse Event | 1( 5.9%) | .( . %) | 1( 3.7%) |
| Death | 6( 35.3%) | 7( 70.0%) | 13( 48.1%) |
| Investigator's Discretion | 1( 5.9%) | .( . %) | 1( 3.7%) |
| Lack Of Efficacy | 7( 41.2%) | 2( 20.0%) | 9( 33.3%) |
| Lost To Follow-Up | 1( 5.9%) | 1( 10.0%) | 2( 7.4%) |
| Withdrew Consent | 1( 5.9%) | .( . %) | 1( 3.7%) |

#### 3.2.2.3 Demographic and Baseline Characteristics

Baseline demographics were generally comparable between 12-week and 24-week treatment arms (Table 27 in appendix). More than half of the subjects were male (78.3%). Overall, the mean age was 58.8 years with 14.8% of subject ≥ 65 years of age. Most subjects were white (88.7%) and a small proportion were black/African American (8.9%). Most subjects had HCV GT-1 (98.5%): GT-1a (70.6%) and GT-1b (27.9%), and five subjects have HCV GT-4 (1.4%). The overall mean HCV RNA level was 6.2 log10 IU/mL 70.9% of subjects have HCV viral load ≥ 800,000 IU/mL at baseline. More than half of subjects (77.2%) were treatment-experienced. More than half of subjects (63.8%) had baseline Body Mass Index (BMI) < 30 kg/m$^2$. Please see Table 27 in the Appendix for details.

Demographic and baseline characteristics for each of the 7 groups were generally comparable between the 12-week and 24-week treatment arms within a given group. Please see Table 28-34 in Appendix for details.



Reference ID: 3884456

### 3.2.2.4 Results and Conclusions

- **Applicant's Primary Efficacy Results:**

The applicant's primary results are listed in Table 5 below. The reviewer agrees with these results with additional explanation below.

**Table 5:** Applicant's Results of SVR12 for Study SOLAR-1 (FAS)

**Table 9-1. GS-US-337-0123: Proportion of Subjects With SVR12 Following Treatment With LDV/SOF+RBV for 12 or 24 Weeks in Subjects With Decompensated (CPT B or CPT C) Cirrhosis (Groups 1 and 2) and Posttransplantation Subjects with Stage F0-F3 Fibrosis; Compensated (CPT A) or Decompensated (CPT B or CPT C) Cirrhosis; or Fibrosing Cholestatic Hepatitis (Groups 3 to 7) (Full Analysis Set)**

| Cohort | Liver Disease Status (Group) | Study Treatment | SVR12[a] (n/N [%]) | 90% CI |
|---|---|---|---|---|
| A | CPT B Cirrhosis (Group 1) | LDV/SOF+RBV 12 Weeks | 26/30 (86.7%) | 72.0% to 95.3% |
| | | LDV/SOF+RBV 24 Weeks | 24/27 (88.9%) | 73.7% to 96.9% |
| | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 12 Weeks | 19/22 (86.4%) | 68.4% to 96.2% |
| | | LDV/SOF+RBV 24 Weeks | 20/23 (87.0%) | 69.6% to 96.3% |
| B | Stage F0-F3 Fibrosis (Group 3) | LDV/SOF+RBV 12 Weeks | 53/55 (96.4%) | 89.0% to 99.4% |
| | | LDV/SOF+RBV 24 Weeks | 55/56 (98.2%) | 91.8% to 99.9% |
| | CPT A Cirrhosis (Group 4) | LDV/SOF+RBV 12 Weeks | 25/26 (96.2%) | 83.0% to 99.8% |
| | | LDV/SOF+RBV 24 Weeks | 24/25 (96.0%) | 82.4% to 99.8% |
| | CPT B Cirrhosis (Group 5) | LDV/SOF+RBV 12 Weeks | 22/26 (84.6%) | 68.2% to 94.6% |
| | | LDV/SOF+RBV 24 Weeks | 23/26 (88.5%) | 72.8% to 96.8% |
| | CPT C Cirrhosis (Group 6) | LDV/SOF+RBV 12 Weeks | 3/5 (60.0%) | 18.9% to 92.4% |
| | | LDV/SOF+RBV 24 Weeks | 3/4 (75.0%) | 24.9% to 98.7% |
| | Fibrosing Cholestatic Hepatitis (Group 7) | LDV/SOF+RBV 12 Weeks | 4/4 (100.0%) | 47.3% to 100.0% |
| | | LDV/SOF+RBV 24 Weeks | 2/2 (100.0%) | 22.4% to 100.0% |

a The SVR12 analysis included all subjects in the Full Analysis Set except those who had undergone transplantation prior to SVR12 (HCV RNA < LLOQ at last visit prior to transplantation).
HCV RNA was analyzed using the Roche COBAS Ampliprep/COBAS Taqman HCV Test, v2.0 with lower limit of quantitation 15 IU/mL.
A subject was a success if their latest observed HCV RNA value in the visit window was < LLOQ, or if they had a missing value for the visit window bracketed by observed HCV RNA values that were termed successes (ie, '< LLOQ TND' or '< LLOQ detected'). TND = target not detected.
All subjects who received a transplantation on study with HCV RNA < LLOQ at last measurement prior to transplantation prior to posttreatment Week 12 visit were excluded from analysis.
The exact 90% CI for the proportion within group and treatment duration was based on the Clopper-Pearson method.
Section 15.1, Tables 11.1-11.4
Source: Table 9-1 in CSR of SOLAR-1.

❖ **Some notes regarding the analyses:**

1) 20 subjects' actual treatment group varied from their randomized group:

Because the CPT score changed from the screening visit to the baseline visit, 20 subjects were randomized to one group (planned treatment group, Trt01p) at screening and were assigned to a



Reference ID: 3884456

different group (actual treatment group, Trt01a) in the analyses. The treatment durations of these 20 subjects, however, did not change. These 20 subjects are listed in Table 35 in the Appendix.

The detailed changes were summarized in the Table 6 below. Nineteen subjects switched groups within the same cohort, and one subject (1039-75602) had a change in the cohort assignment. Two subjects having baseline CPT score of 9 (CPT B) were changed to CPT C groups (group 2 and 4). Because only one subject did not meet SVR12, the reviewer did not conduct any sensitivity analysis. The applicant and reviewer used the actual treatment (Trt01a) for the efficacy analyses.

**Table 6:** The Summary of Changes of 20 Subjects who had Different Planned and Actual Treatment Group for Study SOLAR-1 (FAS)

| Cohort | Planned Group[1] | Actual Group[1] | Number of Subjects | Baseline CPT Score | Baseline MELD Score |
|---|---|---|---|---|---|
| Within Pre-transplant cohort | Group 2 (C) | Group 1 (B) | 5 | 8, 9, 9, 9, 9 | 13, 10, 12, 12, 13, 16 |
| | Group 1 (B) | Group 2 (C) | 1 | 9[2] | 15 |
| Within Post-transplant cohort | Group 4 (A) | Group 5 (B) | 1 | 7 | 6 |
| | Group 4 (A) | Group 3 (F0-F3) | 4 | 5, 6, 6, 7 | 8, 11, 12, 13 |
| | Group 3 (F0-F3) | Group 4 (A) | 2 | 5, 6 | 7, 8 |
| | Group 3 (F0-F3) | Group 5 (B) | 1 | 7 | 13 |
| | Group 5 (B) | Group 3 (F0-F3) | 4 | 5, 5, 6, 7 | 6, 10, 10, 11 |
| | Group 5 (B) | Group 4 (A) | 1 | 5 | 7 |
| Between Cohorts | Group 6 (C) | Group 4 (C) | 1 | 9[2] | 14 |

[1]: The letter in the parentheses is the CPT category of the group.
[2]: CPT=9 belongs to CPT category B, not category C.

2) 25 subjects' baseline CPT category did not match with the group assigned:

There were 25 subjects whose CPT category did not match with the actual treatment group specification (Red in Table 7). Two were among subjects who had different planned and actual treatment assignment mentioned above. If sicker patients were assigned to a less sick group, there was no concern. For example, subjects with CPT C assigned to CPT B group, or subjects with CPT B assigned to the CPT A group would not be concerning. In contrast, concern exists when less sick patients are assigned to sicker groups as this scenario may inflate the SVR12 rate. The only case in Table 7 was group 6. Among these 25 subjects, 12 were assigned to the 24-week treatment arm. There were only five subjects who did not meet SVR12, and three of them in the 12-week treatment arm were in Groups 1, 2 and 5.

In Group 5, two subjects with CPT A at baseline were assigned to the 24-week arm, and one of them met SVR12. Two subjects with CPT C at baseline were assigned to the 12-week arm, and one of them met SVR12. It seems that the impact on SVR12 rate in Group 5 is not a concern.

In Group 6, three subjects with CPT B at baseline all met SVR12. Two of subjects were assigned to the 12-week arm and 1 was assigned to the 24-week arm. By including all available subjects in Group 6, the SVR12 rates were 60% (3/5) in the 12-week arm and 75% (3/4) in the 24-week arm. If excluding those three subjects, the SVR12 rates are 33% (1/3) in and 67% (2/3) in the



Reference ID: 3884456

respective 12-week and 24week arms. Because of small sample sizes, the impact of this CPT category on SVR12 rate cannot be assessed here. As a result, the reviewer will use the actual treatment assignment for the following efficacy analyses.

**Table 7:** The Subjects' Baseline CPT Category and Their Actual Group Assignment for Study SOLAR-1 (FAS)

| Baseline CPT category | Actual Group Assignment | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|
| | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 | Group 6 | Group 7 | |
| CPT A | 1 | | 104 | 47 | 2 | | | 154 |
| CPT B | 54 | 9 | 7 | 4 | 48 | 3 | 5 | 130 |
| CPT C | 4 | 40 | | | 2 | 6 | 1 | 53 |
| Total | 59 | 49 | 111 | 51 | 52 | 9 | 6 | 337 |

Note: from the two notes above, it seems that the CPT score measurement is not stable.

3) 7 subjects had liver transplant during the study:

There were 7 subjects having liver transplant during the study, and 6 of them did not have SVR12 visit and were excluded from the efficacy analyses. Out of these 6 subjects, 5 had liver transplants during the treatment phase and the last available viral load before transplantation was < LLOQ. Another subject had a liver transplantation during the follow-up phase and met SVR2. The reviewer agrees with the applicant's decision to exclude these 6 subjects from the efficacy analyses. Please the Table 36 in Appendix for the list of subjects.

One of those 7 subjects did have a SVR12 visit and was included in the efficacy analyses. The final number of subjects including the efficacy analyses is 331 instead of 337 in FAS.

- **Primary Efficacy Results:**

The primary efficacy results by cohort and by group are listed in Table 8 below. The comparison of the SVR12 rates for 12 weeks and 24 weeks are limited by the fact that there is no formal hypothesis testing or win-criteria pre-specified. The SVR12 rates in the 12-week arm were similar to those in the 24-week arm for all 7 groups. Groups 3 and 4 (compensated cirrhosis) had the highest SVR12 rates (>96%). Groups 1 and 5 (decompensated cirrhosis CPT B) had similar SVR12 rates (85% to 89%). The SVR12 rates (86%) in Group 2 (decompensated cirrhosis CPT C pre-transplant) were numerically higher than those (60%) in Group 6 (decompensated cirrhosis CPT C post-transplant). However it is noted that Group 6 had very limited sample sizes, and the 95% CIs overlapped. Based on these results, it appears that the SVR12 rates between pre- and post-transplant for decompensated cirrhosis CPT B and C subjects are similar.

By combining Group 1 and 2 together, Group 5 and 6 together, and Group 3 and 4 together, the SVR12 rates were presented in Table 9. Table 10 presented the SVR12 rates by combining Groups 1, 2, 5, and 6. The SVR12 rate was **84.3%** with 95% CI of [74.7, 91.4] for decompensated cirrhosis with CPT B or C with 12 weeks of treatment.



Reference ID: 3884456

**Table 8:** Primary Efficacy Results (SVR12) by Group for SOLAR-1 (Efficacy Analysis Set)

| Cohort | Group | T12WK* | T24WK |
|---|---|---|---|
| **A (pre-transplant)** | **G1: CPT B** | **86.7% (26/30) (69.3, 96.2)** | **88.9% (24/27) (70.8, 97.7)** |
| | G2: CPT C | 86.4% (19/22) (65.1, 97.1) | 87.0% (20/23) (66.4, 97.2) |
| B Post-transplant) | G3: F0-F3 Fibrosis | 96.4% (53/55) (87.5, 99.6) | 98.2% (55/56) (90.5, 100.0) |
| | G4: CPT A | 96.2% (25/26) (80.4, 99.9) | 96.0% (24/25) (79.7, 99.9) |
| | **G5: CPT B** | 84.6% (22/26) (65.1, 95.6) | 88.5% (23/26) (69.9, 97.6) |
| | G6: CPT C | 60.0% (3/5) (14.7, 94.7) | 75.0% (3/4) (19.4, 99.4) |
| | G7: FCH | 100% (4/4) (39.8, 100.0) | 100% (2/2) (15.8, 100.0) |

*: SVR12 rate (n/N) and 95% confidence interval (CI).

**Table 9:** SVR12 Rate by Group Combination (Pre vs. Post) for SOLAR-1 (Efficacy Analysis Set)

| Transplant Status | Cirrhosis Status | T12WK* | T24WK |
|---|---|---|---|
| Pre-transplanted (CPT B / C) | Decompensated (G1+G2) | 86.5% (45/52) (74.2, 94.4) | 88.0% (44/50) (75.7, 95.5) |
| Post-transplanted (CPT B / C) | Decompensated (G5+G6) | 80.7% (25/31) (62.5, 92.6) | 86.7% (26/30) (69.3, 96.2) |
| Post-transplanted (CPT A) | Compensated (G3+G4) | 96.3% (78/81) (89.6, 99.2) | 97.5% (79/81) (91.4, 99.7) |

*: SVR12 rate (n/N) and 95% confidence interval (CI).

**Table 10:** SVR12 Rate by Group Combination (CPT Category) for SOLAR-1 (Efficacy Analysis Set)

| CPT Category | Cirrhosis Status | T12WK* | T24WK |
|---|---|---|---|
| CPT B | Decompensated (G1+G5) | 85.7% (48/56) (73.8, 93.6) | 88.7% (47/53) (77.0, 95.7) |
| CPT C | Decompensated (G2+G6) | 81.5% (22/27) (61.9, 93.7) | 85.2% (23/27) (66.3, 95.8) |
| **CPT B/C** | **Decompensated (G1+G5+G2+G6)** | **84.3% (70/83) (74.7, 91.4)** | **87.5% (70/80) (78.2, 93.8)** |

*: SVR12 rate (n/N) and 95% confidence interval (CI).

### 3.2.3 SOLAR-2 (GS-US-337-0124)

#### 3.2.2.1 Patient Disposition

For SOLAR-2, a total of 334 subjects were randomized and 1 subject was not dosed, and was excluded from the Safety and FAS populations. Table 11 describes the subject disposition of subjects in FAS. The majority of treated subjects (95%) completed the designed treatment period and 90% of subjects completed the designed all study visits. Seventeen subjects (5.1%) prematurely discontinued study treatment, mainly due to the adverse event (AE) (7 subjects, 41.2%).



Reference ID: 3884456

**Table 11:** Subjects Disposition for Study SOLAR-2 (FAS)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| N | 167 | 166 | 333 |
| Completed Treatment Period | | | |
| Y | 160( 95.8%) | 156( 94.0%) | 316( 94.9%) |
| N | 7( 4.2%) | 10( 6.0%) | 17( 5.1%) |
| Reasons of NOT completed treatment | | | |
| Adverse Event | 2( 28.6%) | 5( 50.0%) | 7( 41.2%) |
| Death | 2( 28.6%) | 2( 20.0%) | 4( 23.5%) |
| Investigator's Discretion | 1( 14.3%) | 1( 10.0%) | 2( 11.8%) |
| Liver Transplant | 1( 14.3%) | 2( 20.0%) | 3( 17.6%) |
| Non-Compliance With Study Drug | 1( 14.3%) | .( . %) | 1( 5.9%) |
| Completed Study | | | |
| Y | 146( 88.0%) | 120( 92.3%) | 266( 89.9%) |
| N | 20( 12.0%) | 10( 7.7%) | 30( 10.1%) |
| Reasons of NOT completed study | | | |
| Death | 9( 45.0%) | 7( 70.0%) | 16( 53.3%) |
| Lack Of Efficacy | 8( 40.0%) | 2( 20.0%) | 10( 33.3%) |
| Lost To Follow-Up | 2( 10.0%) | .( . %) | 2( 6.7%) |
| Withdrew Consent | 1( 5.0%) | 1( 10.0%) | 2( 6.7%) |

#### 3.2.3.3 Demographic and Baseline Characteristics

Baseline demographics were generally comparable between the 12-week and 24-week treatment arms (Table 37 in appendix). More than half of the subjects were male (75.4%). Overall, the mean age was 58.0 years with 19.8% of subjects ≥ 65 years of age. Most subjects were white (94.3%) and a small proportion were Asian (2.1%) and black/African American (1.5%). Most subjects had HCV GT-1 (88.9%): GT-1a (48.9%) and GT-1b (39.9%), and 37 subjects have HCV GT-4 (11.1%). The overall mean HCV RNA level was 6.2 log10 IU/mL 68.2% of subjects have HCV viral load ≥ 800,000 IU/mL at baseline. More than half of subjects (77.2%) were treatment-experienced. More than half of subjects (79.9%) had baseline BMI index < 30 kg/m$^2$. Please see Table 37 in the Appendix for details.

Most of these demographic and baseline characteristics in SOLAR-2 are similar to what was observed in SOLAR-1 except SOLAR-2 had more GT-4 subjects enrolled.

Demographic and baseline characteristics for each of 7 groups were generally comparable between 12 weeks and 24 weeks treatment arms within a given group. Please see Table 38-44 in Appendix for details.

#### 3.2.3.4 Results and Conclusions

- **<u>Applicant's Primary Efficacy Results:</u>**

The applicant's primary results are listed in Table 12 below. The reviewer agrees with these results with additional explanation below.



Reference ID: 3884456

**Table 12:** Applicant's Results of SVR12 for Study SOLAR-1 (FAS)

**Table 9-2. GS-US-337-0124: Proportion of Subjects With SVR12 by Genotype Following Treatment With LDV/SOF+RBV for 12 or 24 Weeks in Subjects With Decompensated (CPT B or CPT C) Cirrhosis (Groups 1 and 2) and Posttransplantation Subjects with Stage F0-F3 Fibrosis; Compensated (CPT A) or Decompensated (CPT B or CPT C) Cirrhosis; or Fibrosing Cholestatic Hepatitis (Groups 3 to 7) (Full Analysis Set)**

| Cohort | Liver Disease Status (Group) | Study Treatment | Genotype 1 | | Genotype 4 | |
|---|---|---|---|---|---|---|
| | | | SVR12[a] (n/N [%]) | 90% CI | SVR12[a] (n/N [%]) | 90% CI |
| A | CPT B Cirrhosis (Group 1) | LDV/SOF+RBV 12 Weeks | 20/23 (87.0%) | 69.6% to 96.3% | 2/3 (66.7%) | 13.5% to 98.3% |
| | | LDV/SOF+RBV 24 Weeks | 22/23 (95.7%) | 81.0% to 99.8% | 2/2 (100.0%) | 22.4% to 100.0% |
| | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 12 Weeks | 17/20 (85.0%) | 65.6% to 95.8% | 0/1 | 0.0% to 95.0% |
| | | LDV/SOF+RBV 24 Weeks | 18/23 (78.3%) | 59.6% to 91.0% | 1/2 (50.0%) | 2.5% to 97.5% |
| B | Stage F0-F3 Fibrosis (Group 3) | LDV/SOF+RBV 12 Weeks | 42/45 (93.3%) | 83.7% to 98.2% | 7/7 (100.0%) | 65.2% to 100.0% |
| | | LDV/SOF+RBV 24 Weeks | 44/44 (100.0%) | 93.4% to 100.0% | 5/5 (100.0%) | 54.9% to 100.0% |
| | CPT A Cirrhosis (Group 4) | LDV/SOF+RBV 12 Weeks | 30/30 (100.0%) | 90.5% to 100.0% | 3/4 (75.0%) | 24.9% to 98.7% |
| | | LDV/SOF+RBV 24 Weeks | 27/28 (96.4%) | 84.1% to 99.8% | 5/5 (100.0%) | 54.9% to 100.0% |
| | CPT B Cirrhosis (Group 5) | LDV/SOF+RBV 12 Weeks | 19/20 (95.0%) | 78.4% to 99.7% | 2/2 (100.0%) | 22.4% to 100.0% |
| | | LDV/SOF+RBV 24 Weeks | 20/20 (100.0%) | 86.1% to 100.0% | 3/3 (100.0%) | 36.8% to 100.0% |
| | CPT C Cirrhosis (Group 6) | LDV/SOF+RBV 12 Weeks | 1/2 (50.0%) | 2.5% to 97.5% | 0/1 | 0.0% to 95.0% |
| | | LDV/SOF+RBV 24 Weeks | 4/5 (80.0%) | 34.3% to 99.0% | NA | NA |
| | Fibrosing Cholestatic Hepatitis (Group 7) | LDV/SOF+RBV 12 Weeks | 3/3 (100.0%) | 36.8% to 100.0% | NA | NA |
| | | LDV/SOF+RBV 24 Weeks | 2/2 (100.0%) | 22.4% to 100.0% | NA | NA |

a The SVR12 analysis included all subjects in the Full Analysis Set except those who had undergone transplantation prior to SVR12 (HCV RNA < LLOQ at last visit prior to transplantation).
HCV RNA was analyzed using the Roche COBAS Ampliprep/COBAS Taqman HCV Test, v2.0 with a lower limit of quantitation of 15 IU/mL.
A subject was a success if their latest observed HCV RNA value in the visit window was < LLOQ, or if they had a missing value for the visit window bracketed by observed HCV RNA values that were termed successes (ie, '< LLOQ TND' or '< LLOQ detected'). TND = target not detected.
The exact 90% CI for the proportion within group and treatment duration was based on the Clopper-Pearson method.
Source: Section 15.1, Table 13.5-13.8

Source: Table 9-2 in CSR of SOLAR-2.

❖ **Some notes regarding the analyses:**

1) 3 subjects did not have advanced liver disease and did not qualify for Cohort A (screening CPT score: 5, 5, and 6) and were excluded from the FAS analysis population. Two of them were in the 12-week treatment arm of Group 1 and another was in the 24-week treatment arm in Group 1. For these three subjects, their safety flag was "Yes" meaning they were included in the Safety population while the FAS flag was "No" meaning they were excluded from the FAS population. As a result, FAS had 330 subjects.

2) 20 subjects' actual group was not the randomized group:

Because the CPT score changed from the screening visit to the baseline visit, 20 subjects were randomized to one group (planned treatment group, Trt01p) at screening and were assigned to a different group (actual treatment group, Trt01a) in the analyses. The treatment durations of these 20 subjects, however, did not change. These 20 subjects are listed in Table 45 in the Appendix.

The detailed changes were summarized in the Table 13 below. All subjects switched groups within the same cohort. Four subjects' baseline CPT scores still did not match with the Group assigned. Because only two subjects did not meet SVR12 and one of them (GS-US-337-0124-8632-76149) had liver transplant on-treatment without SVR12 visit, the reviewer did not conduct



Reference ID: 3884456

any sensitivity analysis. The applicant and reviewer used the actual treatment (Trt01a) for the efficacy analyses.

**Table 13:** The Summary of Changes of 20 Subjects who had Different Planned and Actual Treatment Group for Study SOLAR-2 (FAS)

| Cohort | Planned Group[1] | Actual Group[1] | Number of Subjects | Baseline CPT Score | Baseline MELD Score |
|---|---|---|---|---|---|
| Within Pre-transplant cohort | Group 2 (C) | Group 1 (B) | 1 | 11 | 14 |
| | Group 1 (B) | Group 2 (C) | 3 | 9[2], 10, 11 | 15, 13, 17 |
| Within Post-transplant cohort | Group 4 (A) | Group 5 (B) | 1 | 6[2] | 9 |
| | Group 4 (A) | Group 3 (F0-F3) | 2 | 5, 6 | 8, 15 |
| | Group 3 (F0-F3) | Group 4 (A) | 3 | 5, 6, 6 | 9, 6, 12 |
| | Group 5 (B) | Group 6 (C) | 2 | 9[2], 10 | 13, 14 |
| | Group 5 (B) | Group 4 (A) | 4 | 6, 6, 6, 6 | 11, 11, 14, 14 |
| | Group 6 (C) | Group 5 (B) | 3 | 8, 9, 11[2] | 10, 12, 18 |
| | Group 7 (FCH) | Group 3 (F0-F3) | 1 | 9 | 19 |

[1]: The letter in the parentheses is the CPT category of the group.
[2]: Subjects' baseline CPT scores still did not match with the group assignment.

3) 19 subjects' baseline CPT category did not match with the group assigned:

There were 19 subjects whose CPT category did not match with the actual treatment group specification (Red in Table 14). Five were among subjects who had different planned and actual treatment assignment mentioned above.

Among these 19 subjects, 7 were assigned to the 24-week treatment arm. There were only two subjects who did not meet SVR12, and these two were in the 12-week treatment arm. As mentioned in study SOLAR-1 section 3.2.2.4, it seems that the CPT score measurement is not stable. As a result, the reviewer uses the actual treatment assignment for the efficacy analyses.

**Table 14:** The Subjects' Baseline CPT Category and Their Actual Group Assignment for Study SOLAR-2 (FAS)

| Baseline CPT category* | Actual Group Assignment | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|
| | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 | Group 6 | Group 7 | |
| CPT A | | | 97 | 66 | 5 | | 1 | 169 |
| CPT B | 51 | 8 | 3 | 1 | 38 | 1 | 3 | 105 |
| CPT C | 2 | 43 | | | 2 | 7 | 1 | 55 |
| Total | 53 | 51 | 100 | 67 | 45 | 8 | 5 | 329 |

*: One subject missed baseline CPT category.

4) 10 subjects had liver transplant during the study:

There were 10 subjects having liver transplants during the study, and 7 did not have SVR12 visit and were excluded from the efficacy analyses. Out of these 7 subjects, 6 had liver transplants during the treatment phase and the last available viral load before transplantation was < LLOQ. Another subject had a liver transplantation during the follow-up phase and met SVR8. The reviewer agrees with the applicant's decision to exclude these 7 subjects from the efficacy analyses. Please the Table 46 in Appendix for the list of subjects.



Reference ID: 3884456

The three transplant subjects who did have a SVR12 visit and were included in the efficacy analyses. The final number of subjects included in the efficacy analyses was 323 instead of the 330 in the FAS.

- **Primary Efficacy Results:**

Out of these 323 subjects in the efficacy analysis population, 288 subjects had GT-1 HCV infection, and 35 had GT-4 HCV infection. This section only presented the SVR12 rates for GT-1 subjects only. The overall SVR12 rate results are listed in Table 47-49 in Appendix.

The SVR12 rates for **GT-1** only by cohort and by group are listed in Table 15 below. The comparison of the SVR12 rates for 12 weeks and 24 weeks are limited by the fact that there is no formal hypothesis testing or win-criteria pre-specified. The SVR12 rates in the 12-week arm were similar to those in the 24-week arm for all 7 groups as seen in SOLAR-1. Groups 3 and 4 (compensated cirrhosis) had the highest SVR12 rates (>93%). Groups 1 and 5 (decompensated cirrhosis CPT B) had similar SVR12 rates (87% to 100%). The SVR12 rates in Group 2 (decompensated cirrhosis CPT C pre-transplant) were similar to that in Group 6 (decompensated cirrhosis CPT C post-transplant). However it is noted that Group 6 had very limited sample sizes, and the 95% CIs overlapped. Based on these results, it appears that the SVR12 rates between pre- and post-transplant for decompensated cirrhosis CPT B and C subjects are similar.

By combining Group 1 and 2 together, Group 5 and 6 together, and Group 3 and 4 together, the SVR12 rates were presented in Table 16. Table 17 presented the SVR12 rates by combining Groups 1, 2, 5, and 6. The SVR12 rate was **87.7%** with 95% CI of [77.2, 94.5] for decompensated cirrhosis with CPT B or C with 12 weeks of treatment.

**Table 15:** Primary Efficacy Results (SVR12) of GT-1 by Group for SOLAR-2 (Efficacy Analysis Set)

| Cohort | Group | T12WK* | T24WK |
|---|---|---|---|
| **A (pre-transplant)** | **G1: CPT B** | **87.0% (20/23) (66.4, 97.2)** | **95.7% (22/23) (78.1, 99.9)** |
| | G2: CPT C | **85.0% (17/20) (62.1, 97.0)** | **78.3% (18/23) (56.3, 92.5)** |
| B (Post-transplant) | G3: F0-F3 Fibrosis | 93.3% (42/45) (81.7, 98.6) | 100% (44/44) (92.0, 100.0) |
| | G4: CPT A | 100% (30/30) (88.4, 100.0) | 96.4% (27/28) (81.7, 99.9) |
| | **G5: CPT B** | **95.0% (19/20) (75.1, 99.9)** | **100% (20/20) (83.2, 100.0)** |
| | **G6: CPT C** | **50.0% (1/2) (1.3, 98.7)** | **80.0% (4/5) (28.4, 99.5)** |
| | G7: FCH | 100% (3/3) (29.2, 100.0) | 100% (2/2) (15.8, 100.0) |

*: SVR12 rate (n/N) and 95% confidence interval (CI).



Reference ID: 3884456

**Table 16:** SVR12 Rate of GT-1 by Group Combination (Pre vs. Post) for SOLAR-2 (Efficacy Analysis Set)

| Transplant Status | Cirrhosis Status | T12WK* | T24WK |
|---|---|---|---|
| Pre-transplanted (CPT B / C) | Decompensated (G1+G2) | 86.1% (37/43) (72.1, 94.7) | 87.0% (40/46) (73.7, 95.1) |
| Post-transplanted (CPT B / C) | Decompensated (G5+G6) | 90.9% (20/22) (70.8, 98.9) | 96.0% (24/25) (79.7, 99.9) |
| Post-transplanted (CPT A) | Compensated (G3+G4) | 96.0% (72/75) (88.8, 99.2) | 98.6% (71/72) (92.5, 100.0) |

*: SVR12 rate (n/N) and 95% confidence interval (CI).

**Table 17:** SVR12 Rate of GT-1 by Group Combination (CPT Category) for SOLAR-2 (Efficacy Analysis Set)

| CPT Category | Cirrhosis Status | T12WK* | T24WK |
|---|---|---|---|
| CPT B | Decompensated (G1+G5) | 90.7% (39/43) (77.9, 97.4) | 97.7% (42/43) (87.7, 99.9) |
| CPT C | Decompensated (G2+G6) | 81.8% (18/22) (59.7, 94.8) | 78.6% (22/28) (59.1, 91.7) |
| **CPT B/C** | **Decompensated (G1+G5+G2+G6)** | **87.7% (57/65) (77.2, 94.5)** | **90.1% (64/71) (80.7, 95.9)** |

*: SVR12 rate (n/N) and 95% confidence interval (CI).

Since SOLAR-1 and SOLAR-2 had identical study designs and had very similar results in terms of SVR12 rates and subgroup analysis by region were very similar, the following section will combine the two studies together for the joint analyses and especially focus on the decompensated cirrhosis groups (ie, Group 1, 2, 5, and 6). These results from the combined studies are proposed by the applicant to be presented in Section 14 of the label. In the following section, the two studies were combined for the final analyses.

### 3.2.4 Combination of SOLAR-1 and SOLAR-2

A total of 670 subjects received the study drug: 337 from SOLAR-1 and 333 from SOLAR-2. Three subjects who did not have advanced liver disease in SOLAR-2 and did not qualify for Cohort A were excluded from the full analysis set. In addition, six subjects in SOLAR-1 and 7 subjects in SOLAR-2 who had liver transplants during the trials and did not have a SVR12 visit were excluded from the efficacy analyses. As a result, the final number of subjects for the efficacy analyses was 654 (329 subjects received 12 weeks of treatment and 325 subjects received 24 weeks of treatment). Out of these 654, 614 subjects (307 subjects received 12 weeks of treatment and 307 subjects received 24 weeks of treatment) had GT-1 HCV infection and 40 subjects (22 subjects received 12 weeks of treatment and 18 subjects received 24 weeks of treatment) had GT-4 HCV infection.

#### 3.2.4.1 Demographic and Baseline Characteristics

Demographics and baseline characteristics were balanced across the treatment groups. Of the 670 treated subjects, the median age was 59 years (range: 21 to 81); 77% of the subjects were male; 50% of subjects were from US; 91% were White; mean body mass index (BMI) was 28 kg/m$^2$ (range: 18 to 49 kg/m$^2$); 72% of subjects' BMI were less than 30kg/m$^2$; 94% and 6% of



Reference ID: 3884456

subjects had genotype 1 and 4 HCV infection, respectively; 78% of the subjects failed a prior HCV therapy. Please see Table 50 in Appendix for details.

Demographics and baseline characteristics by treatment arm for each group separately are listed in Table 51-57 in Appendix for details

#### 3.2.4.2 Results and Conclusions

- **Summary of Applicant's Results**

The applicant's SVR12 results of the two studies combined are listed in Table 18 below. The reviewer agrees with these results.

**Table 18:** Applicant's Results of SVR12 for Combination of SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

**Table 2. Clinical Studies and SVR12 Rates that Support the Efficacy of LDV/SOF for Specific Patient Subpopulations Included in the Summary of Clinical Efficacy**

| | Liver Disease Status (Group) | Duration of Treatment | Genotype 1 | | Genotype 4 | | Overall | |
|---|---|---|---|---|---|---|---|---|
| | | | SVR12 (n/N [%]) | 95% CI | SVR12 (n/N [%]) | 95% CI | SVR12 (n/N [%]) | 95% CI |
| Pretransplantation | CPT B Cirrhosis (Group 1) | 12 Weeks | 45/52 (86.5%) | 74.2% to 94.4% | 3/4 (75.0%) | 19.4% to 99.4% | 48/56 (85.7%) | 73.8% to 93.6% |
| | | 24 Weeks | 46/50 (92.0%) | 80.8% to 97.8% | 2/2 (100.0%) | 15.8% to 100.0% | 48/52 (92.3%) | 81.5% to 97.9% |
| | CPT C Cirrhosis (Group 2) | 12 Weeks | 35/40 (87.5%) | 73.2% to 95.8% | 1/3 (33.3%) | 0.8% to 90.6% | 36/43 (83.7%) | 69.3% to 93.2% |
| | | 24 Weeks | 38/46 (82.6%) | 68.6% to 92.2% | 1/2 (50.0%) | 1.3% to 98.7% | 39/48 (81.3%) | 67.4% to 91.1% |
| Posttransplantation | Stage F0-F3 Fibrosis (Group 3) | 12 Weeks | 94/99 (94.9%) | 88.6% to 98.3% | 8/8 (100.0%) | 63.1% to 100.0% | 102/107 (95.3%) | 89.4% to 98.5% |
| | | 24 Weeks | 99/100 (99.0%) | 94.6% to 100.0% | 5/5 (100.0%) | 47.8% to 100.0% | 104/105 (99.0%) | 94.8% to 100.0% |
| | CPT A Cirrhosis (Group 4) | 12 Weeks | 55/56 (98.2%) | 90.4% to 100.0% | 3/4 (75.0%) | 19.4% to 99.4% | 58/60 (96.7%) | 88.5% to 99.6% |
| | | 24 Weeks | 51/53 (96.2%) | 87.0% to 99.5% | 5/5 (100.0%) | 47.8% to 100.0% | 56/58 (96.6%) | 88.1% to 99.6% |
| | CPT B Cirrhosis (Group 5) | 12 Weeks | 41/46 (89.1%) | 76.4% to 96.4% | 2/2 (100.0%) | 15.8% to 100.0% | 43/48 (89.6%) | 77.3% to 96.5% |
| | | 24 Weeks | 43/45 (95.6%) | 84.9% to 99.5% | 3/4 (75.0%) | 19.4% to 99.4% | 46/49 (93.9%) | 83.1% to 98.7% |
| | CPT C Cirrhosis (Group 6) | 12 Weeks | 4/7 (57.1%) | 18.4% to 90.1% | 0/1 | 0.0% to 97.5% | 4/8 (50.0%) | 15.7% to 84.3% |
| | | 24 Weeks | 7/9 (77.8%) | 40.0% to 97.2% | 0 | — | 7/9 (77.8%) | 40.0% to 97.2% |
| | Fibrosing Cholestatic Hepatitis (Group 7) | 12 Weeks | 7/7 (100.0%) | 59.0% to 100.0% | 0 | — | 7/7 (100.0%) | 59.0% to 100.0% |
| | | 24 Weeks | 4/4 (100.0%) | 39.8% to 100.0% | 0 | — | 4/4 (100.0%) | 39.8% to 100.0% |

Source: Module 1.2 Request for priority review, Table 2.

- **<u>Primary Efficacy Results:</u>**

The SVR12 rates for **GT-1** only by cohort and by group are listed in Table 19 below. The SVR12 rates in the 12-week arm were similar to those in the 24-week arm for all 7 groups with some numeric difference. Groups 3 and 4 (compensated cirrhosis) had the highest SVR12 rates (>95%). Groups 1 and 5 (decompensated cirrhosis CPT B) had similar SVR12 rates (87% to 100%). The SVR12 rates in Group 2 (decompensated cirrhosis CPT C pre-transplant) were similar to that in Group 6 (decompensated cirrhosis CPT C post-transplant). However it is noted that Group 6 had very limited sample sizes, and the 95% CIs overlapped. Based on these results, it appears that the SVR12 rates between pre- and post-transplant for decompensated cirrhosis CPT B and C subjects are similar.



Reference ID: 3884456

By combining Groups 1 and 2 together, Groups 5 and 6 together, and Groups 3 and 4 together, the SVR12 rates were presented in Table 20. Table 21 presented the SVR12 rates by combining Groups 1, 2, 5, and 6. The SVR12 rate was **86.2%** with 95% CI of [79.5, 91.4] for decompensated cirrhosis with CPT B or C with 12 weeks of treatment.

The overall SVR12 rate results are listed in Table 58-60 in Appendix.

**Table 19:** Primary Efficacy Results (SVR12) of GT-1 by Group for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Cohort | Group | T12WK* | T24WK |
|---|---|---|---|
| **A (pre-transplant)** | **G1: CPT B** | **86.5% (45/52) (74.2, 94.4)** | **92.0% (46/50) (80.8, 97.8)** |
| | G2: CPT C | 87.5% (35/40) (73.2, 95.8) | 82.6% (38/46) (68.6, 92.2) |
| B (Post-transplant) | G3: F0-F3 Fibrosis | 95.0% (94/99) (88.6, 98.3) | 99.0% (99/100) (94.6, 100.0) |
| | G4: CPT A | 98.2% (55/56) (90.5, 100.0) | 96.2% (51/53) (87.0, 99.5) |
| | **G5: CPT B** | 89.1% (41/46) (76.4, 96.4) | 95.6% (43/45) (84.9, 99.5) |
| | G6: CPT C | 57.1% (4/7) (18.4, 90.1) | 77.8% (7/9) (40.0, 97.2) |
| | G7: FCH | 100% (7/7) (59.0, 100.0) | 100% (4/4) (39.8, 100.0) |

*: SVR12 rate (n/N) and 95% confidence interval (CI).

**Table 20:** SVR12 Rate of GT-1 by Group Combination (Pre vs. Post) for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Transplant Status | Cirrhosis Status | T12WK* | T24WK |
|---|---|---|---|
| Pre-transplanted (CPT B / C) | Decompensated (G1+G2) | 87.0% (80/92) (78.3, 93.1) | 87.5% (84/96) (79.2, 93.4) |
| Post-transplanted (CPT B / C) | Decompensated (G5+G6) | 84.9% (45/53) (72.4, 93.3) | 92.6% (50/54) (82.1, 97.9) |
| Post-transplanted (CPT A) | Compensated (G3+G4) | 96.1% (149/155) (91.8, 98.6) | 98.0% (150/153) (94.4, 99.6) |

*: SVR12 rate (n/N) and 95% confidence interval (CI).

**Table 21:** SVR12 Rate of GT-1 by Group Combination (CPT Category) for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| CPT Category | Cirrhosis Status | T12WK* | T24WK |
|---|---|---|---|
| CPT B | Decompensated (G1+G5) | 87.8% (86/98) (79.6, 93.5) | 93.7% (89/95) (86.8, 97.7) |
| CPT C | Decompensated (G2+G6) | 83.0% (39/47) (69.2, 92.4) | 81.8% (45/55) (69.1, 90.9) |
| **CPT B/C** | **Decompensated (G1+G5+G2+G6)** | **86.2% (125/145) (79.5, 91.4)** | **89.3% (134/150) (83.3, 93.8)** |

*: SVR12 rate (n/N) and 95% confidence interval (CI).

For the 22 **GT-4** HCV infected subjects who received 12 weeks of treatment, the SVR12 rate was 92% (11/12) for subjects without cirrhosis or with compensated cirrhosis in the post-transplant cohort. Regardless the transplant status, the SVR12 rate was 83% (5/6) for subjects with decompensated cirrhosis CPT B, and the SVR12 rate was 25% (1/4) for subjects with decompensated cirrhosis CPT C (Table 72 and 73 in the Appendix).



Reference ID: 3884456

- **Relapse Rate**

The relapse rates between the 12-week arm and the 24-week arm are generally similar with some numeric difference in Groups 1 and 6 (Table 22 and 23). There was one subject in each treatment arm who withdrew consent and 11 subjects died in each treatment arm. Relapse rates were 8.1% (11/136) and 4.3% (6/140) in subjects who received LDV/SOF+RBV for 12 or 24 weeks, respectively, and the difference in relapse rates was 3.8% with the 95% CI of [−2.1%, 10.2%].

**Table 22:** Relapse Rates of GT-1 by Group in 12 Weeks Arm for SOLAR-1 and SOLAR-2 Combined (Efficacy Analysis Set)

| Cohort/Group (T12WK) | SVR12=Success | Reason of unsuccess (SVR12=failure) | | | |
|---|---|---|---|---|---|
| | | Withdrew Consent | Death | Relapse | Relapse Rate |
| **A (Pre-transplant)** | | | | | |
| G1: CPT B | **86.5% (45/52)** | | 1 | 6 | 11.8% (6/51) |
| G2: CPT C | 87.5% (35/40) | | 3 | 2 | 5.4% (2/37) |
| **B (Post-transplant)** | | | | | |
| G3: F0-F3 | 95.0% (94/99) | | 2 | 3 | 3.1% (3/97) |
| G4: CPT A | 98.2% (55/56) | | 1 | | 0% (0/55) |
| G5: CPT B | **89.1% (41/46)** | 1* | 3 | 1 | 2.4% (1/42) |
| G6: CPT C | **57.1% (4/7)** | | 1 | 2 | 33.3% (2/6) |
| G7: FCH | 100% (7/7) | | | | 0% (0/7) |

**Table 23:** Relapse Rates of GT-1 by Group in 24 Weeks Arm for SOLAR-1 and SOLAR-2 Combined (Efficacy Analysis Set)

| Cohort/Group (T24WK) | SVR12=Success | Reason of unsuccess (SVR12=failure) | | | |
|---|---|---|---|---|---|
| | | Withdrew Consent | Death | Relapse | Relapse Rate |
| **A (Pre-transplant)** | | | | | |
| G1: CPT B | **92.0% (46/50)** | | 2 | 2 | 4.2% (2/48) |
| G2: CPT C | 82.6% (38/46) | 1* | 4 | 3 | 7.3% (3/41) |
| **B (Post-transplant)** | | | | | |
| G3: F0-F3 | 99.0% (99/100) | | | | 0% (0/100) |
| G4: CPT A | 96.2% (51/53) | | 2 | | 0% (0/51) |
| G5: CPT B | 95.6% (43/45) | | 2 | | 0% (0/43) |
| G6: CPT C | 77.8% (7/9) | | 1 | 1 | 12.5% (1/8) |
| G7: FCH | 100% (4/4) | | | | 0% (0/4) |

- **MELD Score Improvement**

(b) (4)

The MELD score analyses here focuses on decompensated groups only (ie, CPT B or CPT C groups regardless the transplant status, either pre- or post-transplant). The applicant's results are listed in Figure 2 and 3 below and the applicant stated that:



Reference ID: 3884456

*Among those who achieved SVR12 with 12 weeks treatment with HARVONI+RBV, 57% (70/123) and 19% (23/123) had an improvement or no change in MELD score from baseline to post-treatment week 12, respectively; of the 32 subjects whose MELD score was ≥ 15 at baseline, 59% (19/32) had a MELD score <15 at post-treatment Week 12.*

Even though the 57% of subjects had MELD score improved, the majority of subjects only had less than 4 point decrease in MELD score from baseline and this type of decrease in MELD score is not clinical meaningful according to the clinical review team.

We request a long-term, follow-up study to collect, analyze and submit data on subjects with cirrhosis including decompensated cirrhosis who achieve sustained virologic response following treatment with a sofosbuvir-based regimen to evaluate durability of virologic response and to characterize clinical outcomes such as progression or regression of liver disease, liver-related mortality, occurrence of hepatocellular carcinoma, or liver failure requiring liver transplantation in Postmarketing Commitment (PMC).

**Figure 5.** **GS-US-337-0123 and GS-US-337-0124: Changes in MELD Scores From Baseline to Posttreatment Week 12 For Subjects with Decompensated (CPT B or CPT C) Cirrhosis Who Had a Baseline MELD Score < 15 and Achieved SVR12 (Full Analysis Set)**

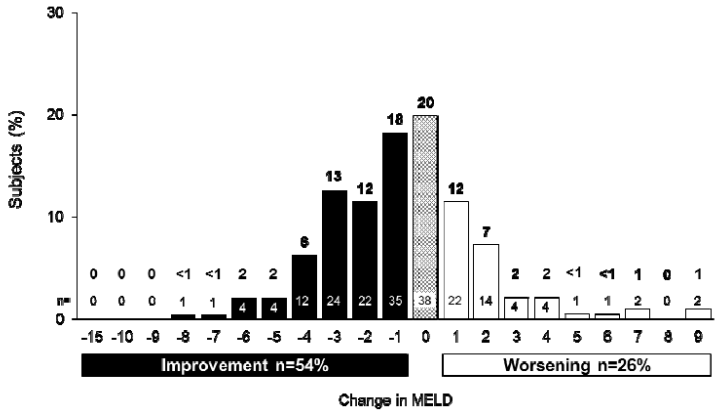


**Figure 2:** The MELD Score Changes at FU-12 from Baseline for Subjects who Had SVR12=Success in Decompensated Groups (Groups 1, 2, 5 and 6) in the Combination of SOLAR-1 and SOLAR-2 (Baseline MELD score<15).
Source: Module 2.7 Clinical Summary Figure 5



Reference ID: 3884456

**Figure 6.** **GS-US-337-0123 and GS-US-337-0124: Changes in MELD Scores From Baseline to Posttreatment Week 12 For Subjects with Decompensated (CPT B or CPT C) Cirrhosis Who Had a Baseline MELD Score ≥ 15 and Achieved SVR12 (Full Analysis Set)**

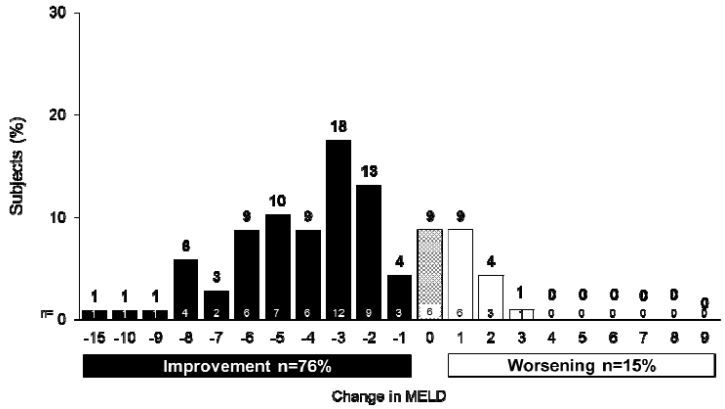


**Figure 3:** The MELD Score Changes at FU-12 from Baseline for Subjects who Had SVR12=Success in Decompensated Groups (Groups 1, 2 , 5 and 6) in the Combination of SOLAR-1 and SOLAR-2 (Baseline MELD score≥15)
Source: Module 2.7 Clinical Summary Figure 6

There were total of 313 subjects in Groups 1, 2, 5, and 6 of the two studies, and 47 subjects either had no MELD score at the baseline visit or at the Follow-Up 12 weeks (FU12) visit. Out of these 266, 127 subjects received 12 weeks of treatment, and 139 subjects received 24 weeks of treatment. Out of these 127 subjects, 120 had GT-1 HCV infection, and 4 of the 127 subjects did not meet SVR 12. Of the latter 4 subjects, 3 had improvement in MELD score (decrease 2 to 4 points) and 1 had MELD score increase by 1 point

In addition, out of the 127 subjects receiving 12 weeks of treatment, 123 subjects met SVR12 and their MELD score changes at the FU12 visit from the baseline visit were calculated. For subjects who met SVR12, the majority of the MELD score changes were within ±3 range for subjects who had MELD score < 15 at the baseline (Figure 4A). If the subjects' MELD score was ≥ 15 at the baseline, a slightly higher proportion of subjects had improved (decreased) MELD scores (Figure 4B). This seems to indicate that the follow-up 12 weeks after the EOT visit is too short to observe clinically significant MELD score improvement from baseline.

As shown in Figure 5, even 24 weeks after the EOT visit did not shown a meaningful clinical improvement of MELD score. Notice that there were only 119 subjects out of these 127 subjects had MELD scores at both the baseline and the FU24 visits. All of them met SVR12.

Please see the Table 61, 62 and 63 in the Appendix for the percentage of subjects having changes in MELD and CPT scores at Follow-Up 12 weeks from baseline in details.



Reference ID: 3884456

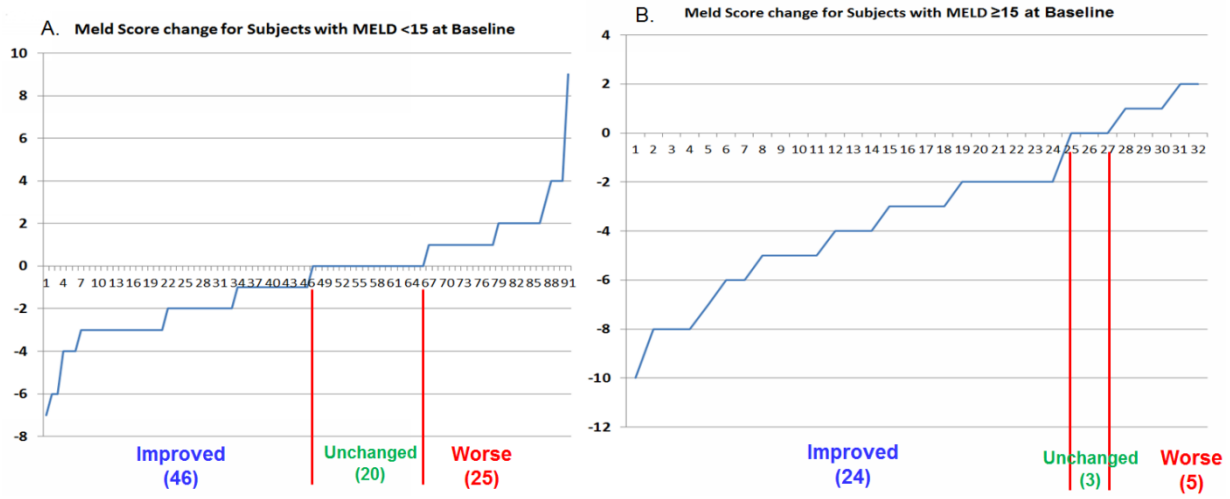


**Figure 4:** The MELD Score Changes at FU-12 Weeks from Baseline for Subjects who Had SVR12=Success in Groups 1, 2, 5, and 6 of SOLAR-1 and SOLAR-2 Combined (A: subjects had MELD<15 at baseline; B: subjects had MELD≥15 at baseline)

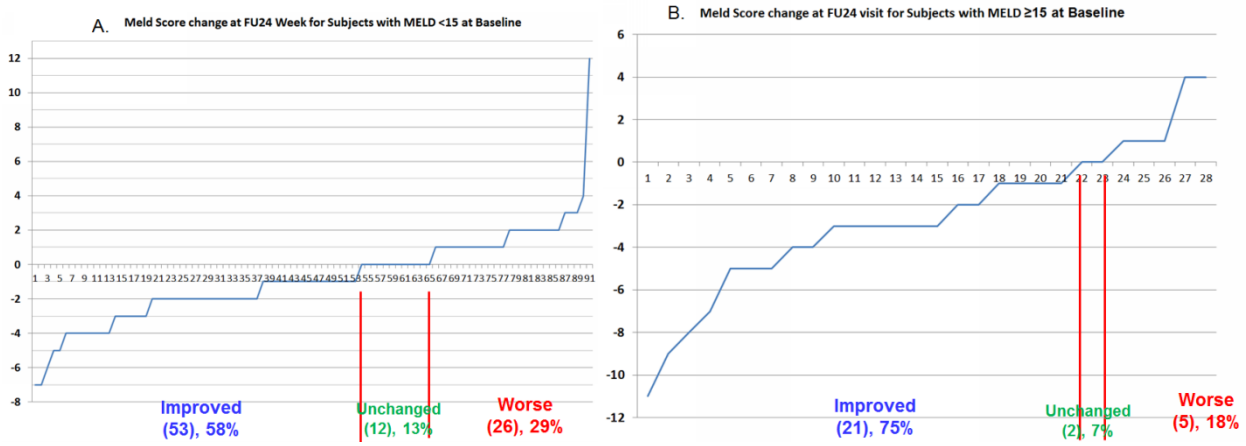


**Figure 5:** The MELD Score Changes at FU-24 Weeks from Baseline for Subjects who Had SVR12=Success in Groups 1, 2, 5, and 6 of SOLAR-1 and SOLAR-2 Combined (A: subjects had MELD<15 at baseline; B: subjects had MELD≥15 at baseline)

### 3.3 Evaluation of Safety

See the clinical review for the evaluation of safety.

## 4. FINDINGS IN SPECIAL/SUBGROUP POPULATIONS

Note that subgroup analyses need to be interpreted with caution because they were post-hoc (with the exception of gender, race, age and geographic region), with no pre-specification or multiple comparison adjustments, had small sample sizes within subgroups, and lacked an active-control.



Reference ID: 3884456

No baseline factors examined here had statistically significant effects on the SVR12 efficacy results within the combined analyses.

The subgroup analyses presented here focus on GT-1 HCV infected subjects in the combination of Groups 3 and 4 (non-cirrhosis and compensated cirrhosis, CPT A) and in the combination of Groups 1, 2, 5, and 6 (decompensated cirrhosis, CPT B/C). The subgroup analyses results for each individual group are listed in Table 64-70 in the Appendix for reference.

### 4.1 Baseline Cirrhosis Status and Genotypes

For the combination of groups 3 and 4 in Table 24, it seems that the SVR12 rate of subjects with baseline MELD score ≥15 (93%) was slightly lower than that of subjects with baseline MELD score <15 (97%). No other baseline factors had significant effects on SVR12.

For the combination of groups 1, 2, 5 and 6 in Table 25, it seems that the SVR12 rate of subjects with baseline MELD score ≥15 (78%) was slightly lower than that of subjects with baseline MELD score ≥10 and <15 (90%). Subjects with baseline MELD score <10 had 100% (46/46) SVR12 rate. No other baseline factors had significant effects on SVR12.

**Table 24**: Subgroup Analysis of SVR12 of GT-1 Subjects for Combination of SOLAR-1 and SOLAR-2 in Group 3 and Group 4 (Efficacy Analysis Set)

| Efficacy Parameter | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 149/155(96.1) | 150/153(98.0) | 299/308(97.1) |
| Gender | | | |
| F | 31 / 32 (96.9) | 29 / 29 ( 100) | 60 / 61 (98.4) |
| M | 118 /123 (95.9) | 121 /124 (97.6) | 239 /247 (96.8) |
| Age Group 1 | | | |
| < 65 | 124 /127 (97.6) | 117 /119 (98.3) | 241 /246 (98.0) |
| >= 65 | 25 / 28 (89.3) | 33 / 34 (97.1) | 58 / 62 (93.5) |
| HCV RNA BSL <800K | | | |
| < 800,000 IU/mL | 34 / 35 (97.1) | 19 / 19 ( 100) | 53 / 54 (98.1) |
| >= 800,000 IU/mL | 115 /120 (95.8) | 131 /134 (97.8) | 246 /254 (96.9) |
| MELD Category at Baseline | | | |
| <10 | 81 / 85 (95.3) | 95 / 96 (99.0) | 176 /181 (97.2) |
| >=10- <15 | 60 / 61 (98.4) | 50 / 52 (96.2) | 110 /113 (97.3) |
| >=15 | 8 / 9 (88.9) | 5 / 5 ( 100) | 13 / 14 (92.9) |
| HCV Genotype | | | |
| 1a | 93 / 98 (94.9) | 97 / 99 (98.0) | 190 /197 (96.4) |
| 1b | 56 / 57 (98.2) | 53 / 54 (98.1) | 109 /111 (98.2) |
| BMI category | | | |
| < 30 kg/m2 | 91 / 96 (94.8) | 117 /119 (98.3) | 208 /215 (96.7) |
| >= 30 kg/m2 | 58 / 59 (98.3) | 33 / 34 (97.1) | 91 / 93 (97.8) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Prior Treatment Category | | | |
| Treatment-experienced | 119 /123 (96.7) | 125 /128 (97.7) | 244 /251 (97.2) |
| Treatment-naive | 30 / 32 (93.8) | 25 / 25 ( 100) | 55 / 57 (96.5) |
| Country | | | |
| AUS | 2 / 2 ( 100) | 5 / 5 ( 100) | 7 / 7 ( 100) |
| AUT | 8 / 8 ( 100) | 4 / 4 ( 100) | 12 / 12 ( 100) |
| BEL | 3 / 3 ( 100) | 4 / 4 ( 100) | 7 / 7 ( 100) |
| CAN | 12 / 12 ( 100) | 10 / 10 ( 100) | 22 / 22 ( 100) |
| CHE | 4 / 5 (80.0) | 5 / 5 ( 100) | 9 / 10 (90.0) |
| DEU | 6 / 6 ( 100) | 8 / 8 ( 100) | 14 / 14 ( 100) |
| ESP | 7 / 8 (87.5) | 11 / 11 ( 100) | 18 / 19 (94.7) |
| FRA | 9 / 10 (90.0) | 7 / 7 ( 100) | 16 / 17 (94.1) |
| GBR | 11 / 11 ( 100) | 11 / 12 (91.7) | 22 / 23 (95.7) |
| ITA | 4 / 4 ( 100) | 2 / 2 ( 100) | 6 / 6 ( 100) |
| NLD | 2 / 2 ( 100) | 2 / 2 ( 100) | 4 / 4 ( 100) |
| NZL | 4 / 4 ( 100) | 2 / 2 ( 100) | 6 / 6 ( 100) |
| USA | 77 / 80 (96.3) | 79 / 81 (97.5) | 156 /161 (96.9) |

**Table 25**: Subgroup Analysis of SVR12 of GT-1 Subjects for Combination of SOLAR-1 and SOLAR-2 in Group 1, Group2, Group 5 and Group 6 (Efficacy Analysis Set)

| Efficacy Parameter | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 125/145(86.2) | 134/150(89.3) | 259/295(87.8) |
| Gender | | | |
| F | 38 / 41 (92.7) | 38 / 42 (90.5) | 76 / 83 (91.6) |
| M | 87 /104 (83.7) | 96 /108 (88.9) | 183 /212 (86.3) |
| Age Group 1 | | | |
| < 65 | 110 /129 (85.3) | 109 /123 (88.6) | 219 /252 (86.9) |
| >= 65 | 15 / 16 (93.8) | 25 / 27 (92.6) | 40 / 43 (93.0) |
| HCV RNA BSL <800K | | | |
| < 800,000 IU/mL | 51 / 59 (86.4) | 55 / 64 (85.9) | 106 /123 (86.2) |
| >= 800,000 IU/mL | 74 / 86 (86.0) | 79 / 86 (91.9) | 153 /172 (89.0) |
| MELD Category at Baseline | | | |
| <10 | 22 / 22 ( 100) | 24 / 24 ( 100) | 46 / 46 ( 100) |
| >=10- <15 | 70 / 80 (87.5) | 75 / 82 (91.5) | 145 /162 (89.5) |
| >=15 | 33 / 43 (76.7) | 35 / 44 (79.5) | 68 / 87 (78.2) |
| HCV Genotype | | | |
| 1a | 80 / 91 (87.9) | 83 / 94 (88.3) | 163 /185 (88.1) |
| 1b | 45 / 54 (83.3) | 51 / 56 (91.1) | 96 /110 (87.3) |
| BMI category | | | |
| < 30 kg/m2 | 85 / 95 (89.5) | 101 /111 (91.0) | 186 /206 (90.3) |
| >= 30 kg/m2 | 40 / 50 (80.0) | 33 / 39 (84.6) | 73 / 89 (82.0) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| CPT Category at Baseline | | | |
| CPT A | 3 / 3 ( 100) | 4 / 4 ( 100) | 7 / 7 ( 100) |
| CPT B | 90 /101 (89.1) | 87 / 94 (92.6) | 177 /195 (90.8) |
| CPT C | 32 / 41 (78.0) | 43 / 52 (82.7) | 75 / 93 (80.6) |
| Country | | | |
| AUS | 9 / 10 (90.0) | 8 / 8 ( 100) | 17 / 18 (94.4) |
| AUT | 3 / 3 ( 100) | 3 / 3 ( 100) | 6 / 6 ( 100) |
| BEL | 3 / 3 ( 100) | 3 / 3 ( 100) | 6 / 6 ( 100) |
| CAN | 12 / 12 ( 100) | 11 / 11 ( 100) | 23 / 23 ( 100) |
| CHE | 2 / 3 (66.7) | 4 / 4 ( 100) | 6 / 7 (85.7) |
| DEU | 4 / 5 (80.0) | 7 / 7 ( 100) | 11 / 12 (91.7) |
| ESP | 10 / 12 (83.3) | 14 / 18 (77.8) | 24 / 30 (80.0) |
| FRA | 4 / 4 ( 100) | 3 / 4 (75.0) | 7 / 8 (87.5) |
| GBR | 3 / 4 (75.0) | 3 / 3 ( 100) | 6 / 7 (85.7) |
| ITA | 4 / 4 ( 100) | 6 / 6 ( 100) | 10 / 10 ( 100) |
| NLD | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| NZL | 2 / 4 (50.0) | 2 / 4 (50.0) | 4 / 8 (50.0) |
| USA | 68 / 80 (85.0) | 70 / 79 (88.6) | 138 /159 (86.8) |

### 4.2 Gender, Race, Age, and Geographic Region

For the combination of Groups 3 and 4, SVR12 rates in combined data were consistent across gender, race and country (Table 24). The SVR12 rate (94%) of subjects with age ≥65 was slightly lower than that of subjects with age <65 years old (98%).

For the combination of Groups 1, 2, 5 and 6, SVR12 rates in combined data were consistent across gender, race and country (Table 25). The SVR12 rate (93%) of subjects with age ≥65 years was slightly higher than that of subjects with age <65 years old (87%).

Please see Table 64-70 for the subgroup analysis results of each individual group of GT-1 HCV infected subjects, Table 71 for the subgroup analysis results of combined group 1, 2, 5 and 6 for GT-1 HCV infected subjects, and Table 73 for GT-4 infected subjects of all 7 groups combined in the Appendix for details.

### 4.3 Other Special/Subgroup Populations

There were 12 principal investigators (PIs) and sub-investigators who had financial interest with the applicant as they reported in application. The sensitivity analyses by excluding subjects enrolled in these sites were conducted. A total of 135 subjects from these PIs out of 654 efficacy analysis set were excluded from the sensitivity analyses. Out of these 519 subjects, 484 GT-1 HCV infected subjects were included in the analyses. The SVR12 rates of both arms, T12WK and T24WK in each group (Table 26) were similar to the overall results presented in Table 19.

Similar results for the group combination of pre- vs. post-transplant and for the group combination of CPT category were observed between with and without those 12 PIs. Please see Table 74-75 in the Appendix for details.



Reference ID: 3884456

**Table 26:** Primary Efficacy Results (SVR12) of GT-1 by Group for SOLAR-1 and SOLAR-2 without 12 Principal Investigators Data (Efficacy Analysis Set)

| Cohort | Group | T12WK* | T24WK |
|---|---|---|---|
| **A (pre-transplant)** | **G1: CPT B** | **87.8% (36/41) (73.8, 95.9)** | **90.0% (36/40) (76.3, 97.2)** |
| | G2: CPT C | 93.8% (30/32) (79.2, 99.2) | 77.1 (27/35) (59.9, 89.6) |
| B (Post-transplant) | G3: F0-F3 Fibrosis | 93.6% (73/78) (85.7, 97.9) | 97.6% (40/41) (87.1, 99.9) |
| | G4: CPT A | 97.8% (44/45) (88.2, 99.9) | 97.6% (40/41) (87.1, 99.9) |
| | **G5: CPT B** | 87.2% (34/39) (72.6, 95.7) | 100% (33/33) (89.4, 100.0) |
| | G6: CPT C | 40.0% (2/5) (5.3, 85.3) | 83.3% (5/6) (35.9, 99.6) |
| | G7: FCH | 100% (6/6) (54.1, 100.0) | 100% (3/3) (29.2, 100.0) |

*: SVR12 rate (n/N) and 95% confidence interval (CI).

# 5. SUMMARY AND CONCLUSIONS

## 5.1 Statistical Issues and Collective Evidence

There were no major statistical issues. Two phase 2 studies were submitted to support the indication.

## 5.2 Conclusions and Recommendations

In conclusion, for 307 GT-1 HCV infected subjects in the 12 weeks treatment arm, the SVR-12 rates for GT-1 HCV infected subjects in the 12-week treatment arm are shown in the Table 19 from the body of the review.

Table 19: SVR12 of GT-1 by Group for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Cohort | Group | T12WK* | T24WK |
|---|---|---|---|
| **A (pre-transplant)** | **G1: CPT B** | **86.5% (45/52) (74.2, 94.4)** | **92.0% (46/50) (80.8, 97.8)** |
| | G2: CPT C | 87.5% (35/40) (73.2, 95.8) | 82.6% (38/46) (68.6, 92.2) |
| B (Post-transplant) | G3: F0-F3 Fibrosis | 95.0% (94/99) (88.6, 98.3) | 99.0% (99/100) (94.6, 100.0) |
| | G4: CPT A | 98.2% (55/56) (90.5, 100.0) | 96.2% (51/53) (87.0, 99.5) |
| | **G5: CPT B** | 89.1% (41/46) (76.4, 96.4) | 95.6% (43/45) (84.9, 99.5) |
| | G6: CPT C | 57.1% (4/7) (18.4, 90.1) | 77.8% (7/9) (40.0, 97.2) |
| | G7: FCH | 100% (7/7) (59.0, 100.0) | 100% (4/4) (39.8, 100.0) |

*: SVR12 rate (n/N) and 95% confidence interval (CI).

The highest SVR12 rates were observed in Group 3 and Group 4 subjects. The SVR12 rate in the decompensated cirrhotic subjects in Groups 1 and 5 was about 87% to 89% regardless of the transplant status. The SVR12 rate in the decompensated cirrhotic subjects in Groups 2 and 6 was 88% in pre-transplant subjects and 57% in pre-transplant subjects. The sample size was limited in Group 6 and the 95% confidence intervals overlapped for the varying treatment durations.



Reference ID: 3884456

The SVR12 rates of the 7 groups in the 24-week treatment arm were very similar to what was observed in the 12-week treatment arm. Although the combined results are presented here, results from the individual studies yielded similar findings.

For the 22 GT-4 HCV infected subjects who received 12 weeks of treatment, the SVR12 rate was 92% (11/12) for subjects without cirrhosis or with compensated cirrhosis in the post-transplant cohort. Regardless the transplant status, the SVR12 rate was 83% (5/6) for subjects with decompensated cirrhosis CPT B, and the SVR12 rate was 25% (1/4) for subjects with decompensated cirrhosis CPT C (Table 72 in the Appendix).

In conclusion, the results from the two studies demonstrated the efficacy of Harvoni plus RBV for 12 weeks in liver transplant GT-1 or GT-4 HCV infected subjects without cirrhosis or with compensated cirrhosis (CPT A), and in GT-1 HCV infected subjects with decompensated cirrhosis (CPT B or C) regardless of the transplant status. As there were no statistical "win" criteria for these studies, the finding of efficacy was primarily based on clinically acceptable SVR12 rates.

## 5.3 Labeling Recommendations

Only SVR12 rates and relapse rates of the 12-week treatment arm for Group 1 to 6 will be presented. The final recommended efficacy table in the label is the following:

Table 16 Studies SOLAR-1 and SOLAR-2: SVR12 and Relapse Rates After 12 Weeks of Treatment with HARVONI and Ribavirin in Subjects with Genotype 1 HCV Who Were Post Liver Transplant and/or Who Had Decompensated Liver Disease.

| | **HARVONI+RBV 12 weeks** | |
|---|---|---|
| | SVR12 (N=300)[a,b] | Relapse (N=288)[a,b,c] |
| Pre-transplant | | |
| CPT B | 87% (45/52) | 12% (6/51) |
| CPT C | 88% (35/40) | 5% (2/37) |
| Post-transplant | | |
| Metavir score F0-F3 | 95% (94/99) | 3% (3/97) |
| CPT A | 98% (55/56) | 0% (0/55) |
| CPT B | 89% (41/46) | 2% (1/42) |
| CPT C | 57% (4/7) | 33% (2/6) |

a. Five subjects transplanted prior to post-treatment Week 12 with HCV RNA<LLOQ at last measurement prior to transplant were excluded.
b. Two subjects were excluded due to failure to meet the inclusion criteria for any of the treatment groups (i.e., did not have decompensated cirrhosis and had also not received a liver transplant).
c. Twelve subjects were excluded from relapse analysis because they died (N=11) or withdrew consent (N=1) prior to reaching the 12 week posttreatment follow-up visit.

Please see the clinical review for details in terms of dosage and administration section of the label.



Reference ID: 3884456

## APPENDICES

**Table 27:** Demographics and Baseline Characteristics for Study SOLAR-1 (FAS)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 169 | 168 | 337 |
| Gender | | | |
| F | 38( 22.5%) | 35( 20.8%) | 73( 21.7%) |
| M | 131( 77.5%) | 133( 79.2%) | 264( 78.3%) |
| Race | | | |
| WHITE | 150( 88.8%) | 149( 88.7%) | 299( 88.7%) |
| BLACK OR AFRICAN AMERICAN | 16( 9.5%) | 14( 8.3%) | 30( 8.9%) |
| AMERICAN INDIAN OR ALASKA NATIVE | 2( 1.2%) | 1( 0.6%) | 3( 0.9%) |
| ASIAN | .( . %) | 1( 0.6%) | 1( 0.3%) |
| OTHER | 1( 0.6%) | 3( 1.8%) | 4( 1.2%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 20( 11.8%) | 18( 10.7%) | 38( 11.3%) |
| NOT HISPANIC OR LATINO | 149( 88.2%) | 150( 89.3%) | 299( 88.7%) |
| Age (Year) | | | |
| Mena (SE) | 58.53 (0.526) | 59.05 (0.537) | 58.79 (0.375) |
| Median | 59.00 | 59.00 | 59.00 |
| Range | (28.00, 78.00) | (21.00, 81.00) | (21.00, 81.00) |
| STD | 6.836 | 6.958 | 6.892 |
| Age Category | | | |
| < 65 | 145( 85.8%) | 142( 84.5%) | 287( 85.2%) |
| >= 65 | 24( 14.2%) | 26( 15.5%) | 50( 14.8%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.16 (0.055) | 6.24 (0.064) | 6.20 (0.042) |
| Median | 6.29 | 6.39 | 6.34 |
| Range | ( 4.07, 7.96) | ( 2.40, 7.83) | ( 2.40, 7.96) |
| STD | 0.719 | 0.826 | 0.774 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 53( 31.4%) | 45( 26.8%) | 98( 29.1%) |
| >= 800,000 IU/mL | 116( 68.6%) | 123( 73.2%) | 239( 70.9%) |
| Baseline Genotype | | | |
| 1a | 118( 69.8%) | 120( 71.4%) | 238( 70.6%) |
| 1b | 47( 27.8%) | 47( 28.0%) | 94( 27.9%) |
| 4 | 1( 0.6%) | 1( 0.6%) | 2( 0.6%) |
| 4a/4c/4d | 2( 1.2%) | .( . %) | 2( 0.6%) |
| 4h | 1( 0.6%) | .( . %) | 1( 0.3%) |
| Baseline BMI (kg/m^2) | | | |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Mean (SE) | 29.32 (0.432) | 28.05 (0.368) | 28.69 (0.285) |
| Median | 28.61 | 27.39 | 27.84 |
| Range | (19.27, 48.53) | (17.59, 45.23) | (17.59, 48.53) |
| STD | 5.610 | 4.766 | 5.238 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 96( 56.8%) | 119( 70.8%) | 215( 63.8%) |
| >= 30 kg/m2 | 73( 43.2%) | 49( 29.2%) | 122( 36.2%) |
| Baseline Cirrhosis Status | | | |
| N | 59( 34.9%) | 58( 34.5%) | 117( 34.7%) |
| Y | 110( 65.1%) | 110( 65.5%) | 220( 65.3%) |
| Baseline ALT | | | |
| Mean (SE) | 82.82 (4.199) | 89.10 (5.719) | 85.95 (3.543) |
| Median | 68.00 | 66.50 | 67.00 |
| Range | (18.00, 271.0) | (12.00, 570.0) | (12.00, 570.0) |
| STD | 54.59 | 74.13 | 65.04 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 73( 43.2%) | 79( 47.0%) | 152( 45.1%) |
| > 1.5 x ULN | 96( 56.8%) | 89( 53.0%) | 185( 54.9%) |
| Baseline CPT Score | | | |
| Mean (SE) | 7.14 (0.150) | 7.09 (0.153) | 7.12 (0.107) |
| Median | 7.00 | 7.00 | 7.00 |
| Range | ( 5.00, 12.00) | ( 5.00, 12.00) | ( 5.00, 12.00) |
| STD | 1.953 | 1.981 | 1.964 |
| Baseline CPT Category | | | |
| CPT A | 76( 45.0%) | 78( 46.4%) | 154( 45.7%) |
| CPT B | 66( 39.1%) | 64( 38.1%) | 130( 38.6%) |
| CPT C | 27( 16.0%) | 26( 15.5%) | 53( 15.7%) |
| Baseline MELD Score | | | |
| Mean (SE) | 11.25 (0.257) | 11.16 (0.287) | 11.20 (0.192) |
| Median | 11.00 | 11.00 | 11.00 |
| Range | ( 6.00, 23.00) | ( 6.00, 21.00) | ( 6.00, 23.00) |
| STD | 3.335 | 3.713 | 3.523 |
| Baseline MELD Category | | | |
| <10 | 58( 34.3%) | 62( 36.9%) | 120( 35.6%) |
| 10-15 | 90( 53.3%) | 80( 47.6%) | 170( 50.4%) |
| 16-20 | 19( 11.2%) | 24( 14.3%) | 43( 12.8%) |
| 21-25 | 2( 1.2%) | 2( 1.2%) | 4( 1.2%) |
| IL28B genotype | | | |
| CC | 33( 19.5%) | 29( 17.3%) | 62( 18.4%) |
| CT | 95( 56.2%) | 98( 58.3%) | 193( 57.3%) |
| TT | 41( 24.3%) | 41( 24.4%) | 82( 24.3%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 124( 73.4%) | 136( 81.0%) | 260( 77.2%) |
| Treatment-naive | 45( 26.6%) | 32( 19.0%) | 77( 22.8%) |
| Prior Response Category | | | |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| n | 124 | 136 | 260 |
| Non-Responder | 81( 65.3%) | 99( 72.8%) | 180( 69.2%) |
| Relapse/Breakthrough | 43( 34.7%) | 37( 27.2%) | 80( 30.8%) |
| **Prior Treatment** | | | |
| n | 124 | 136 | 260 |
| PEG + RBV | 79( 63.7%) | 105( 77.2%) | 184( 70.8%) |
| PI + PEG + RBV | 31( 25.0%) | 23( 16.9%) | 54( 20.8%) |
| Other | 14( 11.3%) | 8( 5.9%) | 22( 8.5%) |
| **Baseline GFR** | | | |
| n | 168 | 167 | 335 |
| Mean (SE) | 71.52 (2.016) | 73.29 (1.820) | 72.40 (1.358) |
| Median | 66.78 | 70.62 | 68.64 |
| Range | (20.44, 165.7) | (26.76, 149.7) | (20.44, 165.7) |
| STD | 26.14 | 23.53 | 24.85 |
| **Country** | | | |
| USA | 169(100.0%) | 168(100.0%) | 337(100.0%) |
| **Region** | | | |
| US | 169(100.0%) | 168(100.0%) | 337(100.0%) |

**Table 28:** Demographics and Baseline Characteristics of Group 1 in Study SOLAR-1 (FAS)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| **Treated (ITT)** | | | |
| N | 30 | 29 | 59 |
| **Gender** | | | |
| F | 8( 26.7%) | 11( 37.9%) | 19( 32.2%) |
| M | 22( 73.3%) | 18( 62.1%) | 40( 67.8%) |
| **Race** | | | |
| WHITE | 29( 96.7%) | 26( 89.7%) | 55( 93.2%) |
| BLACK OR AFRICAN AMERICAN | 1( 3.3%) | 3( 10.3%) | 4( 6.8%) |
| **Ethnicity** | | | |
| HISPANIC OR LATINO | 4( 13.3%) | 3( 10.3%) | 7( 11.9%) |
| NOT HISPANIC OR LATINO | 26( 86.7%) | 26( 89.7%) | 52( 88.1%) |
| **Age (Year)** | | | |
| Mean (SE) | 56.6 (1.67) | 57.8 (1.21) | 57.2 (1.03) |
| Median | 59.5 | 58.0 | 59.0 |
| Range | (28, 69) | (35, 69) | (28, 69) |
| STD | 9.148 | 6.523 | 7.919 |
| **Age Category** | | | |
| < 65 | 27( 90.0%) | 27( 93.1%) | 54( 91.5%) |
| >= 65 | 3( 10.0%) | 2( 6.9%) | 5( 8.5%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 5.85 (0.123) | 5.83 (0.153) | 5.84 (0.097) |
| Median | 6.00 | 6.10 | 6.05 |
| Range | ( 4.28, 6.65) | ( 3.24, 7.12) | ( 3.24, 7.12) |
| STD | 0.676 | 0.822 | 0.745 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 14( 46.7%) | 11( 37.9%) | 25( 42.4%) |
| >= 800,000 IU/mL | 16( 53.3%) | 18( 62.1%) | 34( 57.6%) |
| Baseline Genotype | | | |
| 1a | 19( 63.3%) | 22( 75.9%) | 41( 69.5%) |
| 1b | 10( 33.3%) | 7( 24.1%) | 17( 28.8%) |
| 4a/4c/4d | 1( 3.3%) | .( . %) | 1( 1.7%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 29.16 (1.066) | 29.57 (0.924) | 29.36 (0.701) |
| Median | 27.82 | 29.35 | 28.93 |
| Range | (20.80, 47.00) | (20.94, 45.23) | (20.80, 47.00) |
| STD | 5.839 | 4.974 | 5.388 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 20( 66.7%) | 19( 65.5%) | 39( 66.1%) |
| >= 30 kg/m2 | 10( 33.3%) | 10( 34.5%) | 20( 33.9%) |
| Baseline Cirrhosis Status | | | |
| Y | 30(100.0%) | 29(100.0%) | 59(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 73.40 (5.297) | 79.45 (7.401) | 76.37 (4.504) |
| Median | 67.00 | 73.00 | 68.00 |
| Range | (30.00, 148.0) | (18.00, 184.0) | (18.00, 184.0) |
| STD | 29.01 | 39.86 | 34.60 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 10( 33.3%) | 10( 34.5%) | 20( 33.9%) |
| > 1.5 x ULN | 20( 66.7%) | 19( 65.5%) | 39( 66.1%) |
| Baseline CPT Score | | | |
| Mean (SE) | 8.20 (0.147) | 7.79 (0.175) | 8.00 (0.116) |
| Median | 8.00 | 8.00 | 8.00 |
| Range | ( 7.00, 10.00) | ( 6.00, 10.00) | ( 6.00, 10.00) |
| STD | 0.805 | 0.940 | 0.891 |
| Baseline CPT Category | | | |
| CPT A | .( . %) | 1( 3.4%) | 1( 1.7%) |
| CPT B | 27( 90.0%) | 27( 93.1%) | 54( 91.5%) |
| CPT C | 3( 10.0%) | 1( 3.4%) | 4( 6.8%) |
| Baseline MELD Score | | | |
| Mean (SE) | 11.63 (0.441) | 11.34 (0.573) | 11.49 (0.357) |
| Median | 12.00 | 11.00 | 11.00 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Range | ( 7.00, 16.00) | ( 7.00, 18.00) | ( 7.00, 18.00) |
| STD | 2.414 | 3.085 | 2.744 |
| Baseline MELD Category | | | |
| <10 | 6( 20.0%) | 8( 27.6%) | 14( 23.7%) |
| 10-15 | 21( 70.0%) | 16( 55.2%) | 37( 62.7%) |
| 16-20 | 3( 10.0%) | 5( 17.2%) | 8( 13.6%) |
| IL28B genotype | | | |
| CC | 4( 13.3%) | 5( 17.2%) | 9( 15.3%) |
| CT | 20( 66.7%) | 18( 62.1%) | 38( 64.4%) |
| TT | 6( 20.0%) | 6( 20.7%) | 12( 20.3%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 22( 73.3%) | 19( 65.5%) | 41( 69.5%) |
| Treatment-naive | 8( 26.7%) | 10( 34.5%) | 18( 30.5%) |
| Prior Response Category | | | |
| n | 22 | 19 | 41 |
| Non-Responder | 15( 68.2%) | 14( 73.7%) | 29( 70.7%) |
| Relapse/Breakthrough | 7( 31.8%) | 5( 26.3%) | 12( 29.3%) |
| Prior Treatment | | | |
| n | 22 | 19 | 41 |
| PEG + RBV | 10( 45.5%) | 10( 52.6%) | 20( 48.8%) |
| PI + PEG + RBV | 9( 40.9%) | 9( 47.4%) | 18( 43.9%) |
| Other | 3( 13.6%) | .( . %) | 3( 7.3%) |
| Baseline GFR | | | |
| Mean (SE) | 98.42 (6.449) | 86.25 (5.210) | 92.44 (4.202) |
| Median | 97.79 | 81.15 | 87.94 |
| Range | (33.93, 165.7) | (44.48, 147.7) | (33.93, 165.7) |
| STD | 35.32 | 28.06 | 32.27 |
| Country | | | |
| USA | 30(100.0%) | 29(100.0%) | 59(100.0%) |
| Region | | | |
| US | 30(100.0%) | 29(100.0%) | 59(100.0%) |

**Table 29:** Demographics and Baseline Characteristics of Group 2 in Study SOLAR-1 (FAS)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 23 | 26 | 49 |
| Gender | | | |
| F | 9( 39.1%) | 8( 30.8%) | 17( 34.7%) |
| M | 14( 60.9%) | 18( 69.2%) | 32( 65.3%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Race | | | |
| WHITE | 21( 91.3%) | 24( 92.3%) | 45( 91.8%) |
| BLACK OR AFRICAN AMERICAN | 2( 8.7%) | 1( 3.8%) | 3( 6.1%) |
| OTHER | .( . %) | 1( 3.8%) | 1( 2.0%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 2( 8.7%) | 4( 15.4%) | 6( 12.2%) |
| NOT HISPANIC OR LATINO | 21( 91.3%) | 22( 84.6%) | 43( 87.8%) |
| Age (Year) | | | |
| Mean (SE) | 56.7 (1.30) | 58.54 (0.90) | 57.67 (0.78) |
| median | 58 | 59 | 59 |
| Range | (41, 71) | (48, 68) | (41, 71) |
| STD | 6.23 | 4.61 | 5.45 |
| Age Category | | | |
| < 65 | 22( 95.7%) | 24( 92.3%) | 46( 93.9%) |
| >= 65 | 1( 4.3%) | 2( 7.7%) | 3( 6.1%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 5.59 (0.129) | 5.76 (0.139) | 5.68 (0.095) |
| Median | 5.66 | 5.74 | 5.71 |
| Range | ( 4.07, 6.53) | ( 3.67, 6.88) | ( 3.67, 6.88) |
| STD | 0.618 | 0.707 | 0.666 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 14( 60.9%) | 15( 57.7%) | 29( 59.2%) |
| >= 800,000 IU/mL | 9( 39.1%) | 11( 42.3%) | 20( 40.8%) |
| Baseline Genotype | | | |
| 1a | 15( 65.2%) | 18( 69.2%) | 33( 67.3%) |
| 1b | 6( 26.1%) | 8( 30.8%) | 14( 28.6%) |
| 4a/4c/4d | 1( 4.3%) | .( . %) | 1( 2.0%) |
| 4h | 1( 4.3%) | .( . %) | 1( 2.0%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 31.41 (1.435) | 28.78 (1.115) | 30.01 (0.907) |
| Median | 31.57 | 27.32 | 28.83 |
| Range | (21.18, 48.53) | (19.90, 42.48) | (19.90, 48.53) |
| STD | 6.882 | 5.687 | 6.349 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 10( 43.5%) | 17( 65.4%) | 27( 55.1%) |
| >= 30 kg/m2 | 13( 56.5%) | 9( 34.6%) | 22( 44.9%) |
| Baseline Cirrhosis Status | | | |
| Y | 23(100.0%) | 26(100.0%) | 49(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 57.52 (5.092) | 63.62 (5.545) | 60.76 (3.777) |
| Median | 51.00 | 57.50 | 55.00 |
| Range | (19.00, 126.0) | (21.00, 130.0) | (19.00, 130.0) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| STD | 24.42 | 28.27 | 26.44 |
| **Baseline ALT Category** | | | |
| <= 1.5 x ULN | 15( 65.2%) | 17( 65.4%) | 32( 65.3%) |
| > 1.5 x ULN | 8( 34.8%) | 9( 34.6%) | 17( 34.7%) |
| **Baseline CPT Score** | | | |
| Mean (SE) | 10.22 (0.217) | 10.46 (0.186) | 10.35 (0.142) |
| Median | 10.00 | 10.00 | 10.00 |
| Range | ( 8.00, 12.00) | ( 9.00, 12.00) | ( 8.00, 12.00) |
| STD | 1.043 | 0.948 | 0.991 |
| **Baseline CPT Category** | | | |
| CPT B | 5( 21.7%) | 4( 15.4%) | 9( 18.4%) |
| CPT C | 18( 78.3%) | 22( 84.6%) | 40( 81.6%) |
| **Baseline MELD Score** | | | |
| Mean (SE) | 14.43 (0.461) | 15.46 (0.484) | 14.98 (0.341) |
| Median | 14.00 | 15.50 | 15.00 |
| Range | (11.00, 19.00) | (11.00, 21.00) | (11.00, 21.00) |
| STD | 2.212 | 2.470 | 2.385 |
| **Baseline MELD Category** | | | |
| 10-15 | 16( 69.6%) | 13( 50.0%) | 29( 59.2%) |
| 16-20 | 7( 30.4%) | 12( 46.2%) | 19( 38.8%) |
| 21-25 | .( . %) | 1( 3.8%) | 1( 2.0%) |
| **IL28B genotype** | | | |
| CC | 6( 26.1%) | 7( 26.9%) | 13( 26.5%) |
| CT | 13( 56.5%) | 15( 57.7%) | 28( 57.1%) |
| TT | 4( 17.4%) | 4( 15.4%) | 8( 16.3%) |
| **Prior Treatment Category** | | | |
| Treatment-experienced | 11( 47.8%) | 18( 69.2%) | 29( 59.2%) |
| Treatment-naive | 12( 52.2%) | 8( 30.8%) | 20( 40.8%) |
| **Prior Response Category** | | | |
| n | 11 | 18 | 29 |
| Non-Responder | 7( 63.6%) | 13( 72.2%) | 20( 69.0%) |
| Relapse/Breakthrough | 4( 36.4%) | 5( 27.8%) | 9( 31.0%) |
| **Prior Treatment** | | | |
| n | 11 | 18 | 29 |
| Other | 1( 9.1%) | 1( 5.6%) | 2( 6.9%) |
| PEG + RBV | 8( 72.7%) | 17( 94.4%) | 25( 86.2%) |
| PI + PEG + RBV | 2( 18.2%) | .( . %) | 2( 6.9%) |
| **Baseline GFR** | | | |
| Mean (SE) | 73.69 (4.487) | 85.36 (5.107) | 79.88 (3.499) |
| Median | 76.82 | 78.01 | 77.98 |
| Range | (36.08, 114.4) | (54.10, 149.7) | (36.08, 149.7) |
| STD | 21.52 | 26.04 | 24.50 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Country | | | |
| USA | 23(100.0%) | 26(100.0%) | 49(100.0%) |
| Region | | | |
| US | 23(100.0%) | 26(100.0%) | 49(100.0%) |

**Table 30:** Demographics and Baseline Characteristics of Group 3 in Study SOLAR-1 (FAS)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 55 | 56 | 111 |
| Gender | | | |
| F | 10( 18.2%) | 10( 17.9%) | 20( 18.0%) |
| M | 45( 81.8%) | 46( 82.1%) | 91( 82.0%) |
| Race | | | |
| WHITE | 50( 90.9%) | 49( 87.5%) | 99( 89.2%) |
| BLACK OR AFRICAN AMERICAN | 4( 7.3%) | 4( 7.1%) | 8( 7.2%) |
| AMERICAN INDIAN OR ALASKA NATIVE | 1( 1.8%) | 1( 1.8%) | 2( 1.8%) |
| OTHER | .( . %) | 2( 3.6%) | 2( 1.8%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 4( 7.3%) | 6( 10.7%) | 10( 9.0%) |
| NOT HISPANIC OR LATINO | 51( 92.7%) | 50( 89.3%) | 101( 91.0%) |
| Age (Year) | | | |
| Mean (SE) | 58.82 (0.884) | 58.13 (0.860) | 58.47 (0.614) |
| Median | 59.00 | 58.00 | 59.00 |
| Range | (40.00, 72.00) | (26.00, 69.00) | (26.00, 72.00) |
| STD | 6.555 | 6.433 | 6.473 |
| Age Category | | | |
| < 65 | 46( 83.6%) | 49( 87.5%) | 95( 85.6%) |
| >= 65 | 9( 16.4%) | 7( 12.5%) | 16( 14.4%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.47 (0.083) | 6.40 (0.124) | 6.44 (0.075) |
| Median | 6.63 | 6.65 | 6.65 |
| Range | ( 4.41, 7.68) | ( 2.40, 7.83) | ( 2.40, 7.83) |
| STD | 0.615 | 0.928 | 0.786 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 10( 18.2%) | 10( 17.9%) | 20( 18.0%) |
| >= 800,000 IU/mL | 45( 81.8%) | 46( 82.1%) | 91( 82.0%) |
| Baseline Genotype | | | |
| 1a | 40( 72.7%) | 40( 71.4%) | 80( 72.1%) |
| 1b | 14( 25.5%) | 16( 28.6%) | 30( 27.0%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| 4 | 1( 1.8%) | .( . %) | 1( 0.9%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 29.70 (0.731) | 28.01 (0.572) | 28.84 (0.468) |
| Median | 28.67 | 27.44 | 27.87 |
| Range | (19.76, 47.22) | (21.24, 37.85) | (19.76, 47.22) |
| STD | 5.423 | 4.282 | 4.933 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 31( 56.4%) | 40( 71.4%) | 71( 64.0%) |
| >= 30 kg/m2 | 24( 43.6%) | 16( 28.6%) | 40( 36.0%) |
| Baseline Cirrhosis Status | | | |
| N | 55(100.0%) | 56(100.0%) | 111(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 90.38 (8.966) | 103.2 (12.75) | 96.86 (7.805) |
| Median | 70.00 | 73.50 | 71.00 |
| Range | (18.00, 271.0) | (12.00, 570.0) | (12.00, 570.0) |
| STD | 66.50 | 95.39 | 82.23 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 24( 43.6%) | 23( 41.1%) | 47( 42.3%) |
| > 1.5 x ULN | 31( 56.4%) | 33( 58.9%) | 64( 57.7%) |
| Baseline CPT Score | | | |
| Mean (SE) | 5.38 (0.084) | 5.36 (0.078) | 5.37 (0.057) |
| Median | 5.00 | 5.00 | 5.00 |
| Range | ( 5.00, 7.00) | ( 5.00, 7.00) | ( 5.00, 7.00) |
| STD | 0.623 | 0.586 | 0.602 |
| Baseline CPT Category | | | |
| CPT A | 51( 92.7%) | 53( 94.6%) | 104( 93.7%) |
| CPT B | 4( 7.3%) | 3( 5.4%) | 7( 6.3%) |
| Baseline MELD Score | | | |
| Mean (SE) | 9.76 (0.382) | 8.84 (0.336) | 9.30 (0.257) |
| Median | 10.00 | 8.50 | 9.00 |
| Range | ( 6.00, 18.00) | ( 6.00, 17.00) | ( 6.00, 18.00) |
| STD | 2.835 | 2.514 | 2.706 |
| Baseline MELD Category | | | |
| <10 | 26( 47.3%) | 35( 62.5%) | 61( 55.0%) |
| 10-15 | 25( 45.5%) | 19( 33.9%) | 44( 39.6%) |
| 16-20 | 4( 7.3%) | 2( 3.6%) | 6( 5.4%) |
| Baseline GFR | | | |
| Mean (SE) | 61.84 (2.410) | 69.94 (2.486) | 65.93 (1.766) |
| Median | 60.57 | 71.23 | 64.99 |
| Range | (20.44, 113.3) | (35.26, 116.8) | (20.44, 116.8) |
| STD | 17.87 | 18.60 | 18.61 |
| IL28B genotype | | | |
| CC | 11( 20.0%) | 10( 17.9%) | 21( 18.9%) |
| CT | 33( 60.0%) | 27( 48.2%) | 60( 54.1%) |
| TT | 11( 20.0%) | 19( 33.9%) | 30( 27.0%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Prior Treatment Category | | | |
| Treatment-experienced | 39( 70.9%) | 48( 85.7%) | 87( 78.4%) |
| Treatment-naive | 16( 29.1%) | 8( 14.3%) | 24( 21.6%) |
| Prior Response Category | | | |
| n | 39 | 48 | 87 |
| Non-Responder | 23( 59.0%) | 33( 68.8%) | 56( 64.4%) |
| Relapse/Breakthrough | 16( 41.0%) | 15( 31.3%) | 31( 35.6%) |
| Prior Treatment | | | |
| n | 39 | 48 | 87 |
| Other | 4( 10.3%) | 4( 8.3%) | 8( 9.2%) |
| PEG + RBV | 26( 66.7%) | 39( 81.3%) | 65( 74.7%) |
| PI + PEG + RBV | 9( 23.1%) | 5( 10.4%) | 14( 16.1%) |
| Country | | | |
| USA | 55(100.0%) | 56(100.0%) | 111(100.0%) |
| Region | | | |
| US | 55(100.0%) | 56(100.0%) | 111(100.0%) |

**Table 31:** Demographics and Baseline Characteristics of Group 4 in Study SOLAR-1 (FAS)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 26 | 25 | 51 |
| Gender | | | |
| F | 7( 26.9%) | 3( 12.0%) | 10( 19.6%) |
| M | 19( 73.1%) | 22( 88.0%) | 41( 80.4%) |
| Race | | | |
| WHITE | 21( 80.8%) | 20( 80.0%) | 41( 80.4%) |
| BLACK OR AFRICAN AMERICAN | 3( 11.5%) | 4( 16.0%) | 7( 13.7%) |
| AMERICAN INDIAN OR ALASKA NATIVE | 1( 3.8%) | .( . %) | 1( 2.0%) |
| ASIAN | .( . %) | 1( 4.0%) | 1( 2.0%) |
| OTHER | 1( 3.8%) | .( . %) | 1( 2.0%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 2( 7.7%) | 2( 8.0%) | 4( 7.8%) |
| NOT HISPANIC OR LATINO | 24( 92.3%) | 23( 92.0%) | 47( 92.2%) |
| Age (Year) | | | |
| Mean (SE) | 60.5 (1.22) | 60.7 (2.09) | 60.6 (1.19) |
| Median | 59.5 | 61.0 | 60.00 |
| Range | (49, 78) | (21, 81) | (21, 81) |
| STD | 6.243 | 10.43 | 8.469 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Age Category | | | |
| < 65 | 20( 76.9%) | 17( 68.0%) | 37( 72.5%) |
| >= 65 | 6( 23.1%) | 8( 32.0%) | 14( 27.5%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.19 (0.151) | 6.74 (0.069) | 6.46 (0.092) |
| Median | 6.40 | 6.73 | 6.58 |
| Range | ( 4.57, 7.55) | ( 6.15, 7.53) | ( 4.57, 7.55) |
| STD | 0.772 | 0.345 | 0.657 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 7( 26.9%) | .( . %) | 7( 13.7%) |
| >= 800,000 IU/mL | 19( 73.1%) | 25(100.0%) | 44( 86.3%) |
| Baseline Genotype | | | |
| 1a | 17( 65.4%) | 17( 68.0%) | 34( 66.7%) |
| 1b | 9( 34.6%) | 8( 32.0%) | 17( 33.3%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 29.48 (0.953) | 26.73 (0.912) | 28.13 (0.682) |
| Median | 29.09 | 26.57 | 27.74 |
| Range | (21.16, 41.30) | (17.59, 35.84) | (17.59, 41.30) |
| STD | 4.857 | 4.561 | 4.869 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 14( 53.8%) | 18( 72.0%) | 32( 62.7%) |
| >= 30 kg/m2 | 12( 46.2%) | 7( 28.0%) | 19( 37.3%) |
| Baseline Cirrhosis Status | | | |
| Y | 26(100.0%) | 25(100.0%) | 51(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 85.35 (10.61) | 101.8 (18.37) | 93.41 (10.46) |
| Median | 75.50 | 57.00 | 64.00 |
| Range | (24.00, 238.0) | (17.00, 355.0) | (17.00, 355.0) |
| STD | 54.11 | 91.83 | 74.70 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 11( 42.3%) | 14( 56.0%) | 25( 49.0%) |
| > 1.5 x ULN | 15( 57.7%) | 11( 44.0%) | 26( 51.0%) |
| Baseline CPT Score | | | |
| Mean (SE) | 5.54 (0.114) | 5.80 (0.129) | 5.67 (0.087) |
| median | 5.50 | 6.00 | 6.00 |
| Range | ( 5.00, 7.00) | ( 5.00, 7.00) | ( 5.00, 7.00) |
| STD | 0.582 | 0.645 | 0.622 |
| Baseline CPT Category | | | |
| CPT A | 25( 96.2%) | 22( 88.0%) | 47( 92.2%) |
| CPT B | 1( 3.8%) | 3( 12.0%) | 4( 7.8%) |
| Baseline MELD Score | | | |
| Mean (SE) | 9.81 (0.511) | 9.80 (0.681) | 9.80 (0.419) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Median | 9.00 | 9.00 | 9.00 |
| Range | ( 6.00, 16.00) | ( 6.00, 20.00) | ( 6.00, 20.00) |
| STD | 2.608 | 3.403 | 2.993 |
| Baseline MELD Category | | | |
| <10 | 15( 57.7%) | 13( 52.0%) | 28( 54.9%) |
| 10-15 | 10( 38.5%) | 10( 40.0%) | 20( 39.2%) |
| 16-20 | 1( 3.8%) | 2( 8.0%) | 3( 5.9%) |
| IL28B genotype | | | |
| CC | 7( 26.9%) | 1( 4.0%) | 8( 15.7%) |
| CT | 11( 42.3%) | 19( 76.0%) | 30( 58.8%) |
| TT | 8( 30.8%) | 5( 20.0%) | 13( 25.5%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 22( 84.6%) | 24( 96.0%) | 46( 90.2%) |
| Treatment-naive | 4( 15.4%) | 1( 4.0%) | 5( 9.8%) |
| Prior Response Category | | | |
| n | 22 | 24 | 46 |
| Non-Responder | 14( 63.6%) | 19( 79.2%) | 33( 71.7%) |
| Relapse/Breakthrough | 8( 36.4%) | 5( 20.8%) | 13( 28.3%) |
| Prior Treatment | | | |
| n | 22 | 24 | 46 |
| Other | 4( 18.2%) | 2( 8.3%) | 6( 13.0%) |
| PEG + RBV | 15( 68.2%) | 18( 75.0%) | 33( 71.7%) |
| PI + PEG + RBV | 3( 13.6%) | 4( 16.7%) | 7( 15.2%) |
| Baseline GFR | | | |
| Mean (SE) | 64.12 (3.265) | 71.14 (4.339) | 67.56 (2.719) |
| Median | 59.10 | 67.75 | 62.11 |
| Range | (43.08, 110.9) | (26.76, 109.0) | (26.76, 110.9) |
| STD | 16.65 | 21.69 | 19.42 |
| Country | | | |
| USA | 26(100.0%) | 25(100.0%) | 51(100.0%) |
| Region | | | |
| US | 26(100.0%) | 25(100.0%) | 51(100.0%) |

**Table 32:** Demographics and Baseline Characteristics of Group 5 in Study SOLAR-1 (FAS)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 26 | 26 | 52 |
| Gender | | | |
| F | 4( 15.4%) | 3( 11.5%) | 7( 13.5%) |
| M | 22( 84.6%) | 23( 88.5%) | 45( 86.5%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Race | | | |
| WHITE | 21( 80.8%) | 24( 92.3%) | 45( 86.5%) |
| BLACK OR AFRICAN AMERICAN | 5( 19.2%) | 2( 7.7%) | 7( 13.5%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 5( 19.2%) | 3( 11.5%) | 8( 15.4%) |
| NOT HISPANIC OR LATINO | 21( 80.8%) | 23( 88.5%) | 44( 84.6%) |
| Age (Year) | | | |
| Mean (SE) | 58.9 (1.13) | 61.2 (1.29) | 60.1 (0.87) |
| Median | 60.5 | 61.0 | 61.0 |
| Range | (44, 69) | (37, 72) | (37, 72) |
| STD | 5.77 | 6.59 | 6.25 |
| Age Category | | | |
| < 65 | 23( 88.5%) | 19( 73.1%) | 42( 80.8%) |
| >= 65 | 3( 11.5%) | 7( 26.9%) | 10( 19.2%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.27 (0.109) | 6.24 (0.131) | 6.25 (0.084) |
| Median | 6.39 | 6.41 | 6.39 |
| Range | ( 4.54, 6.96) | ( 4.37, 7.22) | ( 4.37, 7.22) |
| STD | 0.554 | 0.669 | 0.608 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 6( 23.1%) | 9( 34.6%) | 15( 28.8%) |
| >= 800,000 IU/mL | 20( 76.9%) | 17( 65.4%) | 37( 71.2%) |
| Baseline Genotype | | | |
| 1a | 20( 76.9%) | 18( 69.2%) | 38( 73.1%) |
| 1b | 6( 23.1%) | 7( 26.9%) | 13( 25.0%) |
| 4 | .( . %) | 1( 3.8%) | 1( 1.9%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 27.49 (0.879) | 27.54 (0.882) | 27.51 (0.617) |
| Median | 26.36 | 27.02 | 27.02 |
| Range | (19.27, 35.92) | (18.98, 37.79) | (18.98, 37.79) |
| STD | 4.484 | 4.498 | 4.447 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 16( 61.5%) | 20( 76.9%) | 36( 69.2%) |
| >= 30 kg/m2 | 10( 38.5%) | 6( 23.1%) | 16( 30.8%) |
| Baseline Cirrhosis Status | | | |
| Y | 26(100.0%) | 26(100.0%) | 52(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 89.12 (11.95) | 80.27 (11.42) | 84.69 (8.205) |
| Median | 71.00 | 66.50 | 66.50 |
| Range | (27.00, 228.0) | (20.00, 254.0) | (20.00, 254.0) |
| STD | 60.93 | 58.21 | 59.17 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 11( 42.3%) | 12( 46.2%) | 23( 44.2%) |
| > 1.5 x ULN | 15( 57.7%) | 14( 53.8%) | 29( 55.8%) |
| Baseline CPT Score | | | |
| Mean (SE) | 7.81 (0.167) | 7.35 (0.166) | 7.58 (0.121) |
| Median | 8.00 | 7.00 | 7.50 |
| Range | ( 7.00, 10.00) | ( 5.00, 9.00) | ( 5.00, 10.00) |
| STD | 0.849 | 0.846 | 0.871 |
| Baseline CPT Category | | | |
| CPT A | .( . %) | 2( 7.7%) | 2( 3.8%) |
| CPT B | 24( 92.3%) | 24( 92.3%) | 48( 92.3%) |
| CPT C | 2( 7.7%) | .( . %) | 2( 3.8%) |
| Baseline MELD Score | | | |
| Mean (SE) | 11.92 (0.802) | 12.00 (0.610) | 11.96 (0.499) |
| Median | 11.00 | 12.00 | 12.00 |
| Range | ( 6.00, 23.00) | ( 6.00, 20.00) | ( 6.00, 23.00) |
| STD | 4.088 | 3.111 | 3.597 |
| Baseline MELD Category | | | |
| <10 | 8( 30.8%) | 5( 19.2%) | 13( 25.0%) |
| 10-15 | 14( 53.8%) | 19( 73.1%) | 33( 63.5%) |
| 16-20 | 2( 7.7%) | 2( 7.7%) | 4( 7.7%) |
| 21-25 | 2( 7.7%) | .( . %) | 2( 3.8%) |
| IL28B genotype | | | |
| CC | 3( 11.5%) | 5( 19.2%) | 8( 15.4%) |
| CT | 14( 53.8%) | 16( 61.5%) | 30( 57.7%) |
| TT | 9( 34.6%) | 5( 19.2%) | 14( 26.9%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 22( 84.6%) | 22( 84.6%) | 44( 84.6%) |
| Treatment-naive | 4( 15.4%) | 4( 15.4%) | 8( 15.4%) |
| Prior Response Category | | | |
| n | 22 | 22 | 44 |
| Non-Responder | 15( 68.2%) | 16( 72.7%) | 31( 70.5%) |
| Relapse/Breakthrough | 7( 31.8%) | 6( 27.3%) | 13( 29.5%) |
| Prior Treatment | | | |
| n | 22 | 22 | 44 |
| Other | 2( 9.1%) | 1( 4.5%) | 3( 6.8%) |
| PEG + RBV | 12( 54.5%) | 17( 77.3%) | 29( 65.9%) |
| PI + PEG + RBV | 8( 36.4%) | 4( 18.2%) | 12( 27.3%) |
| Baseline GFR | | | |
| Mean (SE) | 68.00 (4.320) | 58.50 (3.024) | 63.25 (2.694) |
| Median | 67.79 | 56.38 | 58.95 |
| Range | (36.70, 118.9) | (29.03, 96.78) | (29.03, 118.9) |
| STD | 22.03 | 15.42 | 19.43 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Country | | | |
| USA | 26(100.0%) | 26(100.0%) | 52(100.0%) |
| Region | | | |
| US | 26(100.0%) | 26(100.0%) | 52(100.0%) |

**Table 33:** Demographics and Baseline Characteristics of Group 6 in Study SOLAR-1 (FAS)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 5 | 4 | 9 |
| Gender | | | |
| M | 5(100.0%) | 4(100.0%) | 9(100.0%) |
| Race | | | |
| WHITE | 4( 80.0%) | 4(100.0%) | 8( 88.9%) |
| BLACK OR AFRICAN AMERICAN | 1( 20.0%) | .( . %) | 1( 11.1%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 3( 60.0%) | .( . %) | 3( 33.3%) |
| NOT HISPANIC OR LATINO | 2( 40.0%) | 4(100.0%) | 6( 66.7%) |
| Age (Year) | | | |
| Mean (SE) | 60.2 (1.68) | 60.7 (0.85) | 60.4 (0.96) |
| Median | 58.0 | 60.5 | 60.0 |
| Range | (57, 66) | (59, 63) | (57, 66) |
| STD | 3.768 | 1.708 | 2.877 |
| Age Category | | | |
| < 65 | 4( 80.0%) | 4(100.0%) | 8( 88.9%) |
| >= 65 | 1( 20.0%) | .( . %) | 1( 11.1%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.36 (0.189) | 6.26 (0.184) | 6.32 (0.126) |
| Median | 6.34 | 6.20 | 6.34 |
| Range | ( 5.76, 6.81) | ( 5.91, 6.73) | ( 5.76, 6.81) |
| STD | 0.422 | 0.368 | 0.378 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 1( 20.0%) | .( . %) | 1( 11.1%) |
| >= 800,000 IU/mL | 4( 80.0%) | 4(100.0%) | 8( 88.9%) |
| Baseline Genotype | | | |
| 1a | 4( 80.0%) | 3( 75.0%) | 7( 77.8%) |
| 1b | 1( 20.0%) | 1( 25.0%) | 2( 22.2%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 29.27 (3.319) | 26.82 (2.767) | 28.18 (2.126) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Median | 31.08 | 24.22 | 24.48 |
| Range | (20.08, 38.73) | (23.74, 35.11) | (20.08, 38.73) |
| STD | 7.421 | 5.534 | 6.377 |
| **Baseline BMI Category (kg/m2)** | | | |
| < 30 kg/m2 | 2( 40.0%) | 3( 75.0%) | 5( 55.6%) |
| >= 30 kg/m2 | 3( 60.0%) | 1( 25.0%) | 4( 44.4%) |
| **Baseline Cirrhosis Status** | | | |
| Y | 5(100.0%) | 4(100.0%) | 9(100.0%) |
| **Baseline ALT** | | | |
| Mean (SE) | 59.80 (12.42) | 79.00 (29.59) | 68.33 (14.15) |
| Median | 75.00 | 82.00 | 75.00 |
| Range | (24.00, 85.00) | (21.00, 131.0) | (21.00, 131.0) |
| STD | 27.76 | 59.17 | 42.44 |
| **Baseline ALT Category** | | | |
| <= 1.5 x ULN | 2( 40.0%) | 2( 50.0%) | 4( 44.4%) |
| > 1.5 x ULN | 3( 60.0%) | 2( 50.0%) | 5( 55.6%) |
| **Baseline CPT Score** | | | |
| Mean (SE) | 9.80 (0.374) | 10.00 (0.408) | 9.89 (0.261) |
| Median | 10.00 | 10.00 | 10.00 |
| Range | ( 9.00, 11.00) | ( 9.00, 11.00) | ( 9.00, 11.00) |
| STD | 0.837 | 0.816 | 0.782 |
| **Baseline CPT Category** | | | |
| CPT B | 2( 40.0%) | 1( 25.0%) | 3( 33.3%) |
| CPT C | 3( 60.0%) | 3( 75.0%) | 6( 66.7%) |
| **Baseline MELD Score** | | | |
| Mean (SE) | 13.00 (1.517) | 16.25 (1.702) | 14.44 (1.203) |
| Median | 13.00 | 15.50 | 15.00 |
| Range | ( 8.00, 17.00) | (13.00, 21.00) | ( 8.00, 21.00) |
| STD | 3.391 | 3.403 | 3.609 |
| **Baseline MELD Category** | | | |
| <10 | 1( 20.0%) | .( . %) | 1( 11.1%) |
| 10-15 | 3( 60.0%) | 2( 50.0%) | 5( 55.6%) |
| 16-20 | 1( 20.0%) | 1( 25.0%) | 2( 22.2%) |
| 21-25 | .( . %) | 1( 25.0%) | 1( 11.1%) |
| **IL28B genotype** | | | |
| CC | 2( 40.0%) | 1( 25.0%) | 3( 33.3%) |
| CT | 2( 40.0%) | 2( 50.0%) | 4( 44.4%) |
| TT | 1( 20.0%) | 1( 25.0%) | 2( 22.2%) |
| **Prior Treatment Category** | | | |
| Treatment-experienced | 4( 80.0%) | 4(100.0%) | 8( 88.9%) |
| Treatment-naive | 1( 20.0%) | .( . %) | 1( 11.1%) |
| **Prior Response Category** | | | |
| n | 4 | 4 | 8 |
| Non-Responder | 3( 75.0%) | 3( 75.0%) | 6( 75.0%) |
| Relapse/Breakthrough | 1( 25.0%) | 1( 25.0%) | 2( 25.0%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Prior Treatment | | | |
| n | 4 | 4 | 8 |
| PEG + RBV | 4(100.0%) | 3( 75.0%) | 7( 87.5%) |
| PI + PEG + RBV | .( . %) | 1( 25.0%) | 1( 12.5%) |
| Baseline GFR | | | |
| Mean (SE) | 62.70 (3.650) | 58.42 (7.138) | 60.80 (3.572) |
| Median | 66.58 | 61.77 | 66.58 |
| Range | (54.00, 72.06) | (39.51, 70.62) | (39.51, 72.06) |
| STD | 8.162 | 14.28 | 10.72 |
| Country | | | |
| USA | 5(100.0%) | 4(100.0%) | 9(100.0%) |
| Region | | | |
| US | 5(100.0%) | 4(100.0%) | 9(100.0%) |

**Table 34:** Demographics and Baseline Characteristics of Group 7 in Study SOLAR-1 (FAS)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 4 | 2 | 6 |
| Gender | | | |
| M | 4(100.0%) | 2(100.0%) | 6(100.0%) |
| Race | | | |
| WHITE | 4(100.0%) | 2(100.0%) | 6(100.0%) |
| Ethnicity | | | |
| NOT HISPANIC OR LATINO | 4(100.0%) | 2(100.0%) | 6(100.0%) |
| Age (Year) | | | |
| MEAN (SE) | 61.7 (1.60) | 58.0 (6.00) | 60.5 (2.01) |
| median | 61.5 | 58.0 | 61.5 |
| Range | (59, 65) | (52, 64) | (52, 65) |
| STD | 3.202 | 8.485 | 4.930 |
| Age Category | | | |
| < 65 | 3( 75.0%) | 2(100.0%) | 5( 83.3%) |
| >= 65 | 1( 25.0%) | .( . %) | 1( 16.7%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.50 (0.619) | 7.06 (0.634) | 6.69 (0.440) |
| median | 6.56 | 7.06 | 6.56 |
| Range | ( 4.94, 7.96) | ( 6.42, 7.69) | ( 4.94, 7.96) |
| STD | 1.237 | 0.897 | 1.077 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| < 800,000 IU/mL | 1( 25.0%) | .( . %) | 1( 16.7%) |
| >= 800,000 IU/mL | 3( 75.0%) | 2(100.0%) | 5( 83.3%) |
| **Baseline Genotype** | | | |
| 1a | 3( 75.0%) | 2(100.0%) | 5( 83.3%) |
| 1b | 1( 25.0%) | .( . %) | 1( 16.7%) |
| **Baseline BMI (kg/m^2)** | | | |
| Mean (SE) | 24.23 (2.153) | 23.17 (0.746) | 23.88 (1.393) |
| median | 22.82 | 23.17 | 23.17 |
| Range | (21.04, 30.24) | (22.42, 23.91) | (21.04, 30.24) |
| STD | 4.305 | 1.056 | 3.413 |
| **Baseline BMI Category (kg/m2)** | | | |
| < 30 kg/m2 | 3( 75.0%) | 2(100.0%) | 5( 83.3%) |
| >= 30 kg/m2 | 1( 25.0%) | .( . %) | 1( 16.7%) |
| **Baseline Cirrhosis Status** | | | |
| N | 4(100.0%) | 2(100.0%) | 6(100.0%) |
| **Baseline ALT** | | | |
| Mean (SE) | 166.5 (15.41) | 141.0 (79.00) | 158.0 (23.24) |
| Median | 158.5 | 141.0 | 158.5 |
| Range | (142.0, 207.0) | (62.00, 220.0) | (62.00, 220.0) |
| STD | 30.82 | 111.7 | 56.92 |
| **Baseline ALT Category** | | | |
| <= 1.5 x ULN | .( . %) | 1( 50.0%) | 1( 16.7%) |
| > 1.5 x ULN | 4(100.0%) | 1( 50.0%) | 5( 83.3%) |
| **Baseline CPT Score** | | | |
| Mean (SE) | 8.50 (0.645) | 8.50 (0.500) | 8.50 (0.428) |
| Median | 8.50 | 8.50 | 8.50 |
| Range | ( 7.00, 10.00) | ( 8.00, 9.00) | ( 7.00, 10.00) |
| STD | 1.291 | 0.707 | 1.049 |
| **Baseline CPT Category** | | | |
| CPT B | 3( 75.0%) | 2(100.0%) | 5( 83.3%) |
| CPT C | 1( 25.0%) | .( . %) | 1( 16.7%) |
| **Baseline MELD Score** | | | |
| n | 3 | 1 | 4 |
| Mean (SE) | 14.00 (2.887) | 15.00 ( . ) | 14.25 (2.056) |
| Median | 14.00 | 15.00 | 14.50 |
| Range | ( 9.00, 19.00) | (15.00, 15.00) | ( 9.00, 19.00) |
| STD | 5.000 | . | 4.113 |
| **Baseline MELD Category** | | | |
| <10 | 2( 50.0%) | 1( 50.0%) | 3( 50.0%) |
| 10-15 | 1( 25.0%) | 1( 50.0%) | 2( 33.3%) |
| 16-20 | 1( 25.0%) | .( . %) | 1( 16.7%) |
| **IL28B genotype** | | | |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| CT | 2( 50.0%) | 1( 50.0%) | 3( 50.0%) |
| TT | 2( 50.0%) | 1( 50.0%) | 3( 50.0%) |
| **Prior Treatment Category** | | | |
| Treatment-experienced | 4(100.0%) | 1( 50.0%) | 5( 83.3%) |
| Treatment-naive | .( . %) | 1( 50.0%) | 1( 16.7%) |
| **Prior Response Category** | | | |
| n | 4 | 1 | 5 |
| Non-Responder | 4(100.0%) | 1(100.0%) | 5(100.0%) |
| **Prior Treatment** | | | |
| n | 4 | 1 | 5 |
| PEG + RBV | 4(100.0%) | 1(100.0%) | 5(100.0%) |
| **Baseline GFR** | | | |
| n | 3 | 1 | 4 |
| Mean (SE) | 72.65 (18.34) | 68.64 ( . ) | 71.65 (13.00) |
| Median | 89.75 | 68.64 | 79.20 |
| Range | (36.00, 92.19) | (68.64, 68.64) | (36.00, 92.19) |
| STD | 31.76 | . | 26.01 |
| **Country** | | | |
| USA | 4(100.0%) | 2(100.0%) | 6(100.0%) |
| **Region** | | | |
| US | 4(100.0%) | 2(100.0%) | 6(100.0%) |



Reference ID: 3884456

**Table 35:** The List of Subjects who had Different Planned and Actual Treatment Group for Study SOLAR-1 (FAS)

The table below contains all subjects who were misrandomized to the incorrect cohort/group.

| Subject ID | Cohort Group Assignment from IWRSRAND | Cohort Group Assignment from RAND |
|---|---|---|
| 0200-75240 | Cohort A Group 2 (24 Weeks of Treatment) | Cohort A Group 1 (24 Weeks of Treatment) |
| 0200-75247 | Cohort A Group 2 (12 Weeks of Treatment) | Cohort A Group 1 (12 Weeks of Treatment) |
| 0200-75453 | Cohort B Group 4 (24 Weeks of Treatment) | Cohort B Group 5 (24 Weeks of Treatment) |
| 0585-75154 | Cohort A Group 1 (24 Weeks of Treatment) | Cohort A Group 2 (24 Weeks of Treatment) |
| 0585-75239 | Cohort A Group 2 (12 Weeks of Treatment) | Cohort A Group 1 (12 Weeks of Treatment) |
| 0585-75529 | Cohort B Group 5 (24 Weeks of Treatment) | Cohort B Group 3 (24 Weeks of Treatment) |
| 1039-75514 | Cohort B Group 5 (24 Weeks of Treatment) | Cohort B Group 4 (24 Weeks of Treatment) |
| 1039-75602 | Cohort B Group 6 (24 Weeks of Treatment) | Cohort A Group 2 (24 Weeks of Treatment) |
| 1249-75446 | Cohort B Group 4 (24 Weeks of Treatment) | Cohort B Group 3 (24 Weeks of Treatment) |
| 2738-75252 | Cohort A Group 2 (12 Weeks of Treatment) | Cohort A Group 1 (12 Weeks of Treatment) |
| 3055-75401 | Cohort B Group 4 (12 Weeks of Treatment) | Cohort B Group 3 (12 Weeks of Treatment) |
| 4969-75441 | Cohort B Group 4 (24 Weeks of Treatment) | Cohort B Group 3 (24 Weeks of Treatment) |
| 5969-75244 | Cohort A Group 2 (24 Weeks of Treatment) | Cohort A Group 1 (24 Weeks of Treatment) |
| 5969-75346 | Cohort B Group 3 (24 Weeks of Treatment) | Cohort B Group 5 (24 Weeks of Treatment) |
| 5969-75524 | Cohort B Group 5 (24 Weeks of Treatment) | Cohort B Group 3 (24 Weeks of Treatment) |
| 6991-75513 | Cohort B Group 5 (24 Weeks of Treatment) | Cohort B Group 3 (24 Weeks of Treatment) |
| 7275-75351 | Cohort B Group 3 (12 Weeks of Treatment) | Cohort B Group 4 (12 Weeks of Treatment) |
| 7275-75362 | Cohort B Group 3 (12 Weeks of Treatment) | Cohort B Group 4 (12 Weeks of Treatment) |
| 7275-75516 | Cohort B Group 5 (12 Weeks of Treatment) | Cohort B Group 3 (12 Weeks of Treatment) |
| 8430-75434 | Cohort B Group 4 (12 Weeks of Treatment) | Cohort B Group 3 (12 Weeks of Treatment) |

Note: IWRS = interactive web response system used to assign subjects to treatment duration (12 or 24 weeks LDV/SOF+RBV) based on cohort/group.

Note: Actual group and treatment duration are those entered in the Randomization (RAND) eCRF at the time of analysis.

**Table 36:** The List of Subjects who had Liver Transplant during the Study for SOLAR-1 (FAS)

| Subject Number | Liver Disease Status (Group) | Study Treatment | Date of Last Dose of Study Drug (Study Day) | Date of Transplantation | Outcome |
|---|---|---|---|---|---|
| 0200-75243 | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 12 Weeks | (b) (6) | | NA[a] |
| 0522-75207 | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 12 Weeks | | | pTVR12 |
| 0585-75241 | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 24 Weeks | | | pTVR12 |
| 0585-75245 | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 24 Weeks | | | pTVR12 |
| 1039-75111 | CPT B Cirrhosis (Group 1) | LDV/SOF+RBV 24 Weeks | | | pTVR12 |
| 1039-75213 | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 24 Weeks | | | pTVR12 |
| 3055-75108 | CPT B Cirrhosis (Group 1) | LDV/SOF+RBV 24 Weeks | | | pTVR12 |

SVR12=empty

SVR12=Y



Reference ID: 3884456

**Table 37:** Demographics and Baseline Characteristics of for Study SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 167 | 166 | 333 |
| Gender | | | |
| F | 41( 24.6%) | 41( 24.7%) | 82( 24.6%) |
| M | 126( 75.4%) | 125( 75.3%) | 251( 75.4%) |
| Race | | | |
| WHITE | 157( 94.0%) | 157( 94.6%) | 314( 94.3%) |
| ASIAN | 1( 0.6%) | 6( 3.6%) | 7( 2.1%) |
| BLACK OR AFRICAN AMERICAN | 3( 1.8%) | 2( 1.2%) | 5( 1.5%) |
| NATIVE HAWAIIAN OR ALASKA NATIVE | 2( 1.2%) | .( . %) | 2( 0.6%) |
| OTHER | 4( 2.4%) | 1( 0.6%) | 5( 1.5%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 22( 13.2%) | 35( 21.1%) | 57( 17.1%) |
| NOT HISPANIC OR LATINO | 145( 86.8%) | 131( 78.9%) | 276( 82.9%) |
| Age (Year) | | | |
| Mean (SE) | 57.5 (0.62) | 58.5 (0.68) | 58.0 (0.46) |
| Median | 58.0 | 59.0 | 58.0 |
| Range | (27, 76) | (23, 79) | (23, 79) |
| STD | 8.050 | 8.705 | 8.387 |
| Age Category | | | |
| < 65 | 138( 82.6%) | 129( 77.7%) | 267( 80.2%) |
| >= 65 | 29( 17.4%) | 37( 22.3%) | 66( 19.8%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.17 (0.054) | 6.22 (0.049) | 6.20 (0.036) |
| Median | 6.23 | 6.29 | 6.27 |
| Range | ( 3.71, 7.99) | ( 3.40, 7.41) | ( 3.40, 7.99) |
| STD | 0.700 | 0.626 | 0.663 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 55( 32.9%) | 51( 30.7%) | 106( 31.8%) |
| >= 800,000 IU/mL | 112( 67.1%) | 115( 69.3%) | 227( 68.2%) |
| Baseline Genotype | | | |
| 1a | 81( 48.5%) | 82( 49.4%) | 163( 48.9%) |
| 1b | 68( 40.7%) | 65( 39.2%) | 133( 39.9%) |
| 4 | 9( 5.4%) | 9( 5.4%) | 18( 5.4%) |
| 4a | 1( 0.6%) | .( . %) | 1( 0.3%) |
| 4a/4c/4d | 6( 3.6%) | 9( 5.4%) | 15( 4.5%) |
| 4e | .( . %) | 1( 0.6%) | 1( 0.3%) |
| 4h | 1( 0.6%) | .( . %) | 1( 0.3%) |
| 4r | 1( 0.6%) | .( . %) | 1( 0.3%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 27.40 (0.397) | 26.64 (0.296) | 27.02 (0.248) |
| Median | 26.57 | 26.21 | 26.51 |
| Range | (17.56, 44.06) | (17.88, 36.95) | (17.56, 44.06) |
| STD | 5.126 | 3.813 | 4.529 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 126( 75.4%) | 140( 84.3%) | 266( 79.9%) |
| >= 30 kg/m2 | 41( 24.6%) | 26( 15.7%) | 67( 20.1%) |
| Baseline Cirrhosis Status | | | |
| N | 55( 32.9%) | 51( 30.7%) | 106( 31.8%) |
| Y | 112( 67.1%) | 115( 69.3%) | 227( 68.2%) |
| Baseline ALT | | | |
| Mean (SE) | 77.58 (4.094) | 82.45 (4.427) | 80.01 (3.013) |
| Median | 60.00 | 68.00 | 64.00 |
| Range | (14.00, 264.0) | (12.00, 354.0) | (12.00, 354.0) |
| STD | 52.91 | 57.04 | 54.98 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 82( 49.1%) | 74( 44.6%) | 156( 46.8%) |
| > 1.5 x ULN | 85( 50.9%) | 92( 55.4%) | 177( 53.2%) |
| Baseline CPT Score | | | |
| n | 165 | 164 | 329 |
| Mean (SE) | 7.01 (0.164) | 7.04 (0.167) | 7.02 (0.117) |
| Median | 6.00 | 6.00 | 6.00 |
| Range | ( 5.00, 12.00) | ( 5.00, 12.00) | ( 5.00, 12.00) |
| STD | 2.108 | 2.139 | 2.120 |
| Baseline CPT Category | | | |
| n | 165 | 164 | 329 |
| CPT A | 85( 51.5%) | 84( 51.2%) | 169( 51.4%) |
| CPT B | 58( 35.2%) | 47( 28.7%) | 105( 31.9%) |
| CPT C | 22( 13.3%) | 33( 20.1%) | 55( 16.7%) |
| Baseline MELD Score | | | |
| n | 165 | 164 | 329 |
| Mean (SE) | 11.43 (0.307) | 11.16 (0.287) | 11.29 (0.210) |
| Median | 11.00 | 11.00 | 11.00 |
| Range | ( 6.00, 24.00) | ( 6.00, 24.00) | ( 6.00, 24.00) |
| STD | 3.950 | 3.680 | 3.814 |
| Baseline MELD Category | | | |
| <10 | 61( 36.5%) | 65( 39.2%) | 126( 37.8%) |
| 10-15 | 78( 46.7%) | 81( 48.8%) | 159( 47.7%) |
| 16-20 | 25( 15.0%) | 17( 10.2%) | 42( 12.6%) |
| 21-25 | 3( 1.8%) | 3( 1.8%) | 6( 1.8%) |
| IL28B genotype | | | |
| CC | 28( 16.8%) | 39( 23.5%) | 67( 20.1%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| CT | 99( 59.3%) | 85( 51.2%) | 184( 55.3%) |
| TT | 40( 24.0%) | 42( 25.3%) | 82( 24.6%) |
| **Prior Treatment Category** | | | |
| Treatment-experienced | 132( 79.0%) | 133( 80.1%) | 265( 79.6%) |
| Treatment-naive | 35( 21.0%) | 33( 19.9%) | 68( 20.4%) |
| **Prior Response Category** | | | |
| n | 130 | 131 | 261 |
| Non-Responder | 94( 72.3%) | 75( 57.3%) | 169( 64.8%) |
| Relapse/Breakthrough | 36( 27.7%) | 56( 42.7%) | 92( 35.2%) |
| **Prior Treatment** | | | |
| n | 132 | 133 | 265 |
| Other | 13( 9.8%) | 12( 9.0%) | 25( 9.4%) |
| PEG + RBV | 98( 74.2%) | 96( 72.2%) | 194( 73.2%) |
| PI + PEG + RBV | 21( 15.9%) | 25( 18.8%) | 46( 17.4%) |
| **Baseline GFR** | | | |
| Mean (SE) | 74.44 (1.990) | 74.93 (2.222) | 74.68 (1.489) |
| Median | 70.58 | 69.25 | 69.96 |
| Range | (29.24, 189.9) | (27.79, 223.6) | (27.79, 223.6) |
| STD | 25.72 | 28.63 | 27.17 |
| **Country** | | | |
| AUS | 13( 7.8%) | 14( 8.4%) | 27( 8.1%) |
| AUT | 14( 8.4%) | 9( 5.4%) | 23( 6.9%) |
| BEL | 8( 4.8%) | 8( 4.8%) | 16( 4.8%) |
| CAN | 26( 15.6%) | 23( 13.9%) | 49( 14.7%) |
| CHE | 12( 7.2%) | 11( 6.6%) | 23( 6.9%) |
| DEU | 12( 7.2%) | 16( 9.6%) | 28( 8.4%) |
| ESP | 21( 12.6%) | 31( 18.7%) | 52( 15.6%) |
| FRA | 16( 9.6%) | 16( 9.6%) | 32( 9.6%) |
| GBR | 18( 10.8%) | 18( 10.8%) | 36( 10.8%) |
| ITA | 13( 7.8%) | 10( 6.0%) | 23( 6.9%) |
| NLD | 4( 2.4%) | 4( 2.4%) | 8( 2.4%) |
| NZL | 10( 6.0%) | 6( 3.6%) | 16( 4.8%) |
| **Region** | | | |
| Non-US | 167(100.0%) | 166(100.0%) | 333(100.0%) |

**Table 38:** Demographics and Baseline Characteristics of Group 1 in Study SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| **Treated (ITT)** | | | |
| N | 28 | 28 | 56 |
| **Gender** | | | |
| F | 5( 17.9%) | 9( 32.1%) | 14( 25.0%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| M | 23( 82.1%) | 19( 67.9%) | 42( 75.0%) |
| Race | | | |
| WHITE | 25( 89.3%) | 28(100.0%) | 53( 94.6%) |
| BLACK OR AFRICAN AMERICAN | 1( 3.6%) | .( . %) | 1( 1.8%) |
| NATIVE HAWAIIAN OR ALASKA NATIVE | 1( 3.6%) | .( . %) | 1( 1.8%) |
| OTHER | 1( 3.6%) | .( . %) | 1( 1.8%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 6( 21.4%) | 6( 21.4%) | 12( 21.4%) |
| NOT HISPANIC OR LATINO | 22( 78.6%) | 22( 78.6%) | 44( 78.6%) |
| Age (Year) | | | |
| Mean (SE) | 55.1 (1.86) | 56.4 (1.62) | 55.7 (1.23) |
| Median | 56.5 | 57.0 | 57.0 |
| Range | (27, 71) | (36, 74) | (27, 74) |
| STD | 9.854 | 8.552 | 9.168 |
| Age Category | | | |
| < 65 | 25( 89.3%) | 24( 85.7%) | 49( 87.5%) |
| >= 65 | 3( 10.7%) | 4( 14.3%) | 7( 12.5%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.05 (0.093) | 5.90 (0.106) | 5.97 (0.071) |
| Median | 6.01 | 5.90 | 5.98 |
| Range | ( 4.73, 6.94) | ( 4.72, 6.95) | ( 4.72, 6.95) |
| STD | 0.492 | 0.562 | 0.528 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 11( 39.3%) | 14( 50.0%) | 25( 44.6%) |
| >= 800,000 IU/mL | 17( 60.7%) | 14( 50.0%) | 31( 55.4%) |
| Baseline Genotype | | | |
| 1a | 13( 46.4%) | 12( 42.9%) | 25( 44.6%) |
| 1b | 12( 42.9%) | 13( 46.4%) | 25( 44.6%) |
| 4 | .( . %) | 2( 7.1%) | 2( 3.6%) |
| 4a | 1( 3.6%) | .( . %) | 1( 1.8%) |
| 4a/4c/4d | 1( 3.6%) | 1( 3.6%) | 2( 3.6%) |
| 4r | 1( 3.6%) | .( . %) | 1( 1.8%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 27.49 (0.688) | 26.98 (0.686) | 27.23 (0.483) |
| Median | 26.97 | 26.39 | 26.64 |
| Range | (20.22, 35.18) | (20.03, 35.63) | (20.03, 35.63) |
| STD | 3.641 | 3.630 | 3.611 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 23( 82.1%) | 23( 82.1%) | 46( 82.1%) |
| >= 30 kg/m2 | 5( 17.9%) | 5( 17.9%) | 10( 17.9%) |
| Baseline Cirrhosis Status | | | |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Y | 28(100.0%) | 28(100.0%) | 56(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 70.25 (7.830) | 74.93 (7.139) | 72.59 (5.259) |
| Median | 55.00 | 67.00 | 62.50 |
| Range | (33.00, 221.0) | (14.00, 184.0) | (14.00, 221.0) |
| STD | 41.43 | 37.78 | 39.35 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 17( 60.7%) | 11( 39.3%) | 28( 50.0%) |
| > 1.5 x ULN | 11( 39.3%) | 17( 60.7%) | 28( 50.0%) |
| Baseline CPT Score | | | |
| n | 26 | 27 | 53 |
| Mean (SE) | 8.04 (0.162) | 8.19 (0.177) | 8.11 (0.119) |
| Median | 8.00 | 8.00 | 8.00 |
| Range | ( 7.00, 10.00) | ( 7.00, 11.00) | ( 7.00, 11.00) |
| STD | 0.824 | 0.921 | 0.870 |
| Baseline CPT Category | | | |
| n | 26 | 27 | 53 |
| CPT B | 25( 96.2%) | 26( 96.3%) | 51( 96.2%) |
| CPT C | 1( 3.8%) | 1( 3.7%) | 2( 3.8%) |
| Baseline MELD Score | | | |
| n | 26 | 27 | 53 |
| Mean (SE) | 12.88 (0.427) | 11.93 (0.536) | 12.40 (0.347) |
| Median | 13.00 | 12.00 | 12.00 |
| Range | ( 9.00, 17.00) | ( 6.00, 16.00) | ( 6.00, 17.00) |
| STD | 2.179 | 2.786 | 2.529 |
| Baseline MELD Category | | | |
| <10 | 3( 10.7%) | 6( 21.4%) | 9( 16.1%) |
| 10-15 | 21( 75.0%) | 18( 64.3%) | 39( 69.6%) |
| 16-20 | 4( 14.3%) | 4( 14.3%) | 8( 14.3%) |
| IL28B genotype | | | |
| CC | 6( 21.4%) | 9( 32.1%) | 15( 26.8%) |
| CT | 18( 64.3%) | 10( 35.7%) | 28( 50.0%) |
| TT | 4( 14.3%) | 9( 32.1%) | 13( 23.2%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 25( 89.3%) | 24( 85.7%) | 49( 87.5%) |
| Treatment-naive | 3( 10.7%) | 4( 14.3%) | 7( 12.5%) |
| Prior Response Category | | | |
| n | 24 | 23 | 47 |
| Non-Responder | 20( 83.3%) | 13( 56.5%) | 33( 70.2%) |
| Relapse/Breakthrough | 4( 16.7%) | 10( 43.5%) | 14( 29.8%) |
| Prior Treatment | | | |
| n | 25 | 24 | 49 |
| Other | 2( 8.0%) | 1( 4.2%) | 3( 6.1%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| PEG + RBV | 19( 76.0%) | 20( 83.3%) | 39( 79.6%) |
| PI + PEG + RBV | 4( 16.0%) | 3( 12.5%) | 7( 14.3%) |
| Baseline GFR | | | |
| Mean (SE) | 97.75 (6.700) | 92.97 (5.454) | 95.36 (4.292) |
| Median | 89.68 | 91.51 | 90.83 |
| Range | (36.80, 189.9) | (37.40, 164.2) | (36.80, 189.9) |
| STD | 35.45 | 28.86 | 32.12 |
| Country | | | |
| AUS | 1( 3.6%) | 1( 3.6%) | 2( 3.6%) |
| AUT | 2( 7.1%) | 2( 7.1%) | 4( 7.1%) |
| BEL | 1( 3.6%) | 2( 7.1%) | 3( 5.4%) |
| CAN | 6( 21.4%) | 5( 17.9%) | 11( 19.6%) |
| CHE | 1( 3.6%) | 4( 14.3%) | 5( 8.9%) |
| DEU | 2( 7.1%) | 4( 14.3%) | 6( 10.7%) |
| ESP | 6( 21.4%) | 5( 17.9%) | 11( 19.6%) |
| FRA | 1( 3.6%) | 1( 3.6%) | 2( 3.6%) |
| GBR | 5( 17.9%) | 3( 10.7%) | 8( 14.3%) |
| ITA | 2( 7.1%) | 1( 3.6%) | 3( 5.4%) |
| NZL | 1( 3.6%) | .( . %) | 1( 1.8%) |
| Region | | | |
| Non-US | 28(100.0%) | 28(100.0%) | 56(100.0%) |

**Table 39:** Demographics and Baseline Characteristics of Group 2 in Study SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 25 | 26 | 51 |
| Gender | | | |
| F | 10( 40.0%) | 6( 23.1%) | 16( 31.4%) |
| M | 15( 60.0%) | 20( 76.9%) | 35( 68.6%) |
| Race | | | |
| WHITE | 23( 92.0%) | 25( 96.2%) | 48( 94.1%) |
| BLACK OR AFRICAN AMERICAN | 1( 4.0%) | 1( 3.8%) | 2( 3.9%) |
| OTHER | 1( 4.0%) | .( . %) | 1( 2.0%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 3( 12.0%) | 8( 30.8%) | 11( 21.6%) |
| NOT HISPANIC OR LATINO | 22( 88.0%) | 18( 69.2%) | 40( 78.4%) |
| Age (Year) | | | |
| Mean (SE) | 58.4 (1.62) | 54.5 (2.09) | 56.4 (1.35) |
| Median | 58.0 | 50.0 | 57.0 |
| Range | (39, 74) | (40, 79) | (39, 79) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| STD | 8.114 | 10.65 | 9.606 |
| **Age Category** | | | |
| < 65 | 20( 80.0%) | 21( 80.8%) | 41( 80.4%) |
| >= 65 | 5( 20.0%) | 5( 19.2%) | 10( 19.6%) |
| **Baseline HCV RNA log10 (IU/mL)** | | | |
| Mean (SE) | 5.63 (0.117) | 5.71 (0.086) | 5.67 (0.072) |
| Median | 5.66 | 5.75 | 5.69 |
| Range | ( 4.36, 6.77) | ( 4.63, 6.52) | ( 4.36, 6.77) |
| STD | 0.584 | 0.437 | 0.511 |
| **Baseline HCV RNA Category 1 (IU/mL)** | | | |
| < 800,000 IU/mL | 16( 64.0%) | 17( 65.4%) | 33( 64.7%) |
| >= 800,000 IU/mL | 9( 36.0%) | 9( 34.6%) | 18( 35.3%) |
| **Baseline Genotype** | | | |
| 1a | 13( 52.0%) | 12( 46.2%) | 25( 49.0%) |
| 1b | 11( 44.0%) | 11( 42.3%) | 22( 43.1%) |
| 4 | 1( 4.0%) | .( . %) | 1( 2.0%) |
| 4a/4c/4d | .( . %) | 2( 7.7%) | 2( 3.9%) |
| 4e | .( . %) | 1( 3.8%) | 1( 2.0%) |
| **Baseline BMI (kg/m^2)** | | | |
| Mean (SE) | 28.81 (1.297) | 27.53 (0.764) | 28.16 (0.743) |
| Median | 27.07 | 27.94 | 27.12 |
| Range | (19.49, 44.06) | (18.67, 36.39) | (18.67, 44.06) |
| STD | 6.483 | 3.893 | 5.307 |
| **Baseline BMI Category (kg/m2)** | | | |
| < 30 kg/m2 | 19( 76.0%) | 20( 76.9%) | 39( 76.5%) |
| >= 30 kg/m2 | 6( 24.0%) | 6( 23.1%) | 12( 23.5%) |
| **Baseline Cirrhosis Status** | | | |
| Y | 25(100.0%) | 26(100.0%) | 51(100.0%) |
| **Baseline ALT** | | | |
| Mean (SE) | 61.64 (7.181) | 66.12 (5.900) | 63.92 (4.594) |
| Median | 53.00 | 55.50 | 54.00 |
| Range | (18.00, 184.0) | (30.00, 146.0) | (18.00, 184.0) |
| STD | 35.90 | 30.08 | 32.81 |
| **Baseline ALT Category** | | | |
| <= 1.5 x ULN | 13( 52.0%) | 16( 61.5%) | 29( 56.9%) |
| > 1.5 x ULN | 12( 48.0%) | 10( 38.5%) | 22( 43.1%) |
| **Baseline CPT Score** | | | |
| Mean (SE) | 10.40 (0.216) | 10.42 (0.138) | 10.41 (0.126) |
| Median | 11.00 | 10.00 | 10.00 |
| Range | ( 9.00, 12.00) | ( 9.00, 12.00) | ( 9.00, 12.00) |
| STD | 1.080 | 0.703 | 0.898 |
| **Baseline CPT Category** | | | |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| CPT B | 7( 28.0%) | 1( 3.8%) | 8( 15.7%) |
| CPT C | 18( 72.0%) | 25( 96.2%) | 43( 84.3%) |
| **Baseline MELD Score** | | | |
| Mean (SE) | 15.40 (0.770) | 15.62 (0.666) | 15.51 (0.503) |
| Median | 15.00 | 14.50 | 15.00 |
| Range | ( 8.00, 23.00) | (10.00, 24.00) | ( 8.00, 24.00) |
| STD | 3.851 | 3.395 | 3.591 |
| **Baseline MELD Category** | | | |
| <10 | 2( 8.0%) | .( . %) | 2( 3.9%) |
| 10-15 | 11( 44.0%) | 15( 57.7%) | 26( 51.0%) |
| 16-20 | 10( 40.0%) | 9( 34.6%) | 19( 37.3%) |
| 21-25 | 2( 8.0%) | 2( 7.7%) | 4( 7.8%) |
| **IL28B genotype** | | | |
| CC | 7( 28.0%) | 4( 15.4%) | 11( 21.6%) |
| CT | 10( 40.0%) | 15( 57.7%) | 25( 49.0%) |
| TT | 8( 32.0%) | 7( 26.9%) | 15( 29.4%) |
| **Prior Treatment Category** | | | |
| Treatment-experienced | 13( 52.0%) | 18( 69.2%) | 31( 60.8%) |
| Treatment-naive | 12( 48.0%) | 8( 30.8%) | 20( 39.2%) |
| **Prior Response Category** | | | |
| n | 12 | 18 | 30 |
| Non-Responder | 10( 83.3%) | 11( 61.1%) | 21( 70.0%) |
| Relapse/Breakthrough | 2( 16.7%) | 7( 38.9%) | 9( 30.0%) |
| **Prior Treatment** | | | |
| n | 13 | 18 | 31 |
| Other | 1( 7.7%) | 2( 11.1%) | 3( 9.7%) |
| PEG + RBV | 9( 69.2%) | 13( 72.2%) | 22( 71.0%) |
| PI + PEG + RBV | 3( 23.1%) | 3( 16.7%) | 6( 19.4%) |
| **Baseline GFR** | | | |
| Mean (SE) | 78.65 (4.502) | 96.28 (7.798) | 87.64 (4.672) |
| Median | 76.63 | 95.85 | 82.58 |
| Range | (42.16, 132.6) | (42.09, 223.6) | (42.09, 223.6) |
| STD | 22.51 | 39.76 | 33.36 |
| **Country** | | | |
| AUS | 7( 28.0%) | 4( 15.4%) | 11( 21.6%) |
| AUT | 1( 4.0%) | .( . %) | 1( 2.0%) |
| BEL | 3( 12.0%) | .( . %) | 3( 5.9%) |
| CAN | 4( 16.0%) | 1( 3.8%) | 5( 9.8%) |
| CHE | 1( 4.0%) | 2( 7.7%) | 3( 5.9%) |
| DEU | 3( 12.0%) | 3( 11.5%) | 6( 11.8%) |
| ESP | 2( 8.0%) | 7( 26.9%) | 9( 17.6%) |
| FRA | 1( 4.0%) | 4( 15.4%) | 5( 9.8%) |
| GBR | .( . %) | 1( 3.8%) | 1( 2.0%) |
| ITA | 2( 8.0%) | 1( 3.8%) | 3( 5.9%) |
| NZL | 1( 4.0%) | 3( 11.5%) | 4( 7.8%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Region | | | |
| Non-US | 25(100.0%) | 26(100.0%) | 51(100.0%) |

**Table 40:** Demographics and Baseline Characteristics of Group 3 in Study SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 52 | 49 | 101 |
| Gender | | | |
| F | 11( 21.2%) | 10( 20.4%) | 21( 20.8%) |
| M | 41( 78.8%) | 39( 79.6%) | 80( 79.2%) |
| Race | | | |
| WHITE | 50( 96.2%) | 47( 95.9%) | 97( 96.0%) |
| ASIAN | .( . %) | 1( 2.0%) | 1( 1.0%) |
| BLACK OR AFRICAN AMERICAN | 1( 1.9%) | .( . %) | 1( 1.0%) |
| OTHER | 1( 1.9%) | 1( 2.0%) | 2( 2.0%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 4( 7.7%) | 8( 16.3%) | 12( 11.9%) |
| NOT HISPANIC OR LATINO | 48( 92.3%) | 41( 83.7%) | 89( 88.1%) |
| Age (Year) | | | |
| Mean (SE) | 58.1 (1.09) | 58.8 (0.98) | 58.4 (0.73) |
| Median | 57.5 | 60.0 | 59.0 |
| Range | (32, 70) | (44, 73) | (32, 73) |
| STD | 7.868 | 6.850 | 7.363 |
| Age Category | | | |
| < 65 | 40( 76.9%) | 42( 85.7%) | 82( 81.2%) |
| >= 65 | 12( 23.1%) | 7( 14.3%) | 19( 18.8%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.36 (0.100) | 6.50 (0.062) | 6.43 (0.060) |
| Median | 6.55 | 6.57 | 6.55 |
| Range | ( 3.80, 7.53) | ( 5.45, 7.39) | ( 3.80, 7.53) |
| STD | 0.722 | 0.436 | 0.602 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 12( 23.1%) | 5( 10.2%) | 17( 16.8%) |
| >= 800,000 IU/mL | 40( 76.9%) | 44( 89.8%) | 84( 83.2%) |
| Baseline Genotype | | | |
| 1a | 27( 51.9%) | 29( 59.2%) | 56( 55.4%) |
| 1b | 18( 34.6%) | 15( 30.6%) | 33( 32.7%) |
| 4 | 4( 7.7%) | 2( 4.1%) | 6( 5.9%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| 4a/4c/4d | 2( 3.8%) | 3( 6.1%) | 5( 5.0%) |
| 4h | 1( 1.9%) | .( . %) | 1( 1.0%) |
| **Baseline BMI (kg/m^2)** | | | |
| Mean (SE) | 27.50 (0.718) | 25.97 (0.534) | 26.76 (0.456) |
| Median | 26.38 | 25.92 | 26.01 |
| Range | (19.38, 40.83) | (17.88, 35.18) | (17.88, 40.83) |
| STD | 5.180 | 3.741 | 4.582 |
| **Baseline BMI Category (kg/m2)** | | | |
| < 30 kg/m2 | 38( 73.1%) | 44( 89.8%) | 82( 81.2%) |
| >= 30 kg/m2 | 14( 26.9%) | 5( 10.2%) | 19( 18.8%) |
| **Baseline Cirrhosis Status** | | | |
| N | 52(100.0%) | 49(100.0%) | 101(100.0%) |
| **Baseline ALT** | | | |
| Mean (SE) | 76.85 (7.882) | 86.84 (10.70) | 81.69 (6.576) |
| Median | 61.00 | 63.00 | 62.00 |
| Range | (16.00, 235.0) | (21.00, 354.0) | (16.00, 354.0) |
| STD | 56.84 | 74.93 | 66.09 |
| **Baseline ALT Category** | | | |
| <= 1.5 x ULN | 26( 50.0%) | 25( 51.0%) | 51( 50.5%) |
| > 1.5 x ULN | 26( 50.0%) | 24( 49.0%) | 50( 49.5%) |
| **Baseline CPT Score** | | | |
| n | 52 | 48 | 100 |
| Mean (SE) | 5.33 (0.102) | 5.10 (0.045) | 5.22 (0.058) |
| Median | 5.00 | 5.00 | 5.00 |
| Range | ( 5.00, 9.00) | ( 5.00, 6.00) | ( 5.00, 9.00) |
| STD | 0.734 | 0.309 | 0.579 |
| **Baseline CPT Category** | | | |
| n | 52 | 48 | 100 |
| CPT A | 49( 94.2%) | 48(100.0%) | 97( 97.0%) |
| CPT B | 3( 5.8%) | .( . %) | 3( 3.0%) |
| **Baseline MELD Score** | | | |
| n | 52 | 48 | 100 |
| Mean (SE) | 9.67 (0.505) | 8.73 (0.318) | 9.22 (0.306) |
| Median | 9.00 | 8.50 | 9.00 |
| Range | ( 6.00, 24.00) | ( 6.00, 15.00) | ( 6.00, 24.00) |
| STD | 3.639 | 2.200 | 3.057 |
| **Baseline MELD Category** | | | |
| <10 | 32( 61.5%) | 34( 69.4%) | 66( 65.3%) |
| 10-15 | 16( 30.8%) | 15( 30.6%) | 31( 30.7%) |
| 16-20 | 3( 5.8%) | .( . %) | 3( 3.0%) |
| 21-25 | 1( 1.9%) | .( . %) | 1( 1.0%) |
| **IL28B genotype** | | | |
| CC | 9( 17.3%) | 10( 20.4%) | 19( 18.8%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| CT | 31( 59.6%) | 25( 51.0%) | 56( 55.4%) |
| TT | 12( 23.1%) | 14( 28.6%) | 26( 25.7%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 41( 78.8%) | 36( 73.5%) | 77( 76.2%) |
| Treatment-naive | 11( 21.2%) | 13( 26.5%) | 24( 23.8%) |
| Prior Response Category | | | |
| n | 41 | 35 | 76 |
| Non-Responder | 28( 68.3%) | 16( 45.7%) | 44( 57.9%) |
| Relapse/Breakthrough | 13( 31.7%) | 19( 54.3%) | 32( 42.1%) |
| Prior Treatment | | | |
| n | 41 | 36 | 77 |
| Other | 1( 2.4%) | 2( 5.6%) | 3( 3.9%) |
| PEG + RBV | 35( 85.4%) | 24( 66.7%) | 59( 76.6%) |
| PI + PEG + RBV | 5( 12.2%) | 10( 27.8%) | 15( 19.5%) |
| Baseline GFR | | | |
| Mean (SE) | 64.65 (2.191) | 65.79 (2.338) | 65.20 (1.593) |
| Median | 60.88 | 65.74 | 62.37 |
| Range | (33.65, 101.5) | (34.39, 107.3) | (33.65, 107.3) |
| STD | 15.80 | 16.37 | 16.01 |
| Country | | | |
| AUS | .( . %) | 2( 4.1%) | 2( 2.0%) |
| AUT | 8( 15.4%) | 2( 4.1%) | 10( 9.9%) |
| BEL | 3( 5.8%) | 3( 6.1%) | 6( 5.9%) |
| CAN | 8( 15.4%) | 6( 12.2%) | 14( 13.9%) |
| CHE | 4( 7.7%) | 3( 6.1%) | 7( 6.9%) |
| DEU | 6( 11.5%) | 5( 10.2%) | 11( 10.9%) |
| ESP | 4( 7.7%) | 8( 16.3%) | 12( 11.9%) |
| FRA | 4( 7.7%) | 5( 10.2%) | 9( 8.9%) |
| GBR | 8( 15.4%) | 9( 18.4%) | 17( 16.8%) |
| ITA | 2( 3.8%) | 2( 4.1%) | 4( 4.0%) |
| NLD | 3( 5.8%) | 4( 8.2%) | 7( 6.9%) |
| NZL | 2( 3.8%) | .( . %) | 2( 2.0%) |
| Region | | | |
| Non-US | 52(100.0%) | 49(100.0%) | 101(100.0%) |

**Table 41:** Demographics and Baseline Characteristics of Group 4 in Study SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 34 | 33 | 67 |
| Gender | | | |
| F | 6( 17.6%) | 7( 21.2%) | 13( 19.4%) |
| M | 28( 82.4%) | 26( 78.8%) | 54( 80.6%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Race | | | |
| WHITE | 33( 97.1%) | 30( 90.9%) | 63( 94.0%) |
| ASIAN | .( . %) | 3( 9.1%) | 3( 4.5%) |
| NATIVE HAWAIIAN OR ALASKA NATIVE | 1( 2.9%) | .( . %) | 1( 1.5%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 5( 14.7%) | 7( 21.2%) | 12( 17.9%) |
| NOT HISPANIC OR LATINO | 29( 85.3%) | 26( 78.8%) | 55( 82.1%) |
| Age (Year) | | | |
| Mean (SE) | 57.2 (1.24) | 61.9 (1.30) | 59.5 (0.93) |
| Median | 57.5 | 62.0 | 59.0 |
| Range | (33, 73) | (46, 74) | (33, 74) |
| STD | 7.216 | 7.467 | 7.646 |
| Age Category | | | |
| < 65 | 29( 85.3%) | 20( 60.6%) | 49( 73.1%) |
| >= 65 | 5( 14.7%) | 13( 39.4%) | 18( 26.9%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.34 (0.099) | 6.46 (0.095) | 6.40 (0.069) |
| Median | 6.36 | 6.52 | 6.41 |
| Range | ( 4.96, 7.32) | ( 4.68, 7.41) | ( 4.68, 7.41) |
| STD | 0.577 | 0.548 | 0.562 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 9( 26.5%) | 5( 15.2%) | 14( 20.9%) |
| >= 800,000 IU/mL | 25( 73.5%) | 28( 84.8%) | 53( 79.1%) |
| Baseline Genotype | | | |
| 1a | 14( 41.2%) | 13( 39.4%) | 27( 40.3%) |
| 1b | 16( 47.1%) | 15( 45.5%) | 31( 46.3%) |
| 4 | 3( 8.8%) | 2( 6.1%) | 5( 7.5%) |
| 4a/4c/4d | 1( 2.9%) | 3( 9.1%) | 4( 6.0%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 27.08 (0.909) | 27.05 (0.712) | 27.07 (0.575) |
| Median | 27.06 | 26.22 | 26.64 |
| Range | (18.72, 43.46) | (20.52, 36.95) | (18.72, 43.46) |
| STD | 5.299 | 4.091 | 4.707 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 24( 70.6%) | 27( 81.8%) | 51( 76.1%) |
| >= 30 kg/m2 | 10( 29.4%) | 6( 18.2%) | 16( 23.9%) |
| Baseline Cirrhosis Status | | | |
| Y | 34(100.0%) | 33(100.0%) | 67(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 95.41 (10.81) | 84.42 (9.173) | 90.00 (7.084) |
| Median | 65.00 | 80.00 | 76.00 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Range | (23.00, 264.0) | (26.00, 259.0) | (23.00, 264.0) |
| STD | 63.02 | 52.70 | 57.99 |
| **Baseline ALT Category** | | | |
| <= 1.5 x ULN | 13( 38.2%) | 11( 33.3%) | 24( 35.8%) |
| > 1.5 x ULN | 21( 61.8%) | 22( 66.7%) | 43( 64.2%) |
| **Baseline CPT Score** | | | |
| Mean (SE) | 5.41 (0.096) | 5.33 (0.083) | 5.37 (0.063) |
| Median | 5.00 | 5.00 | 5.00 |
| Range | ( 5.00, 7.00) | ( 5.00, 6.00) | ( 5.00, 7.00) |
| STD | 0.557 | 0.479 | 0.517 |
| **Baseline CPT Category** | | | |
| CPT A | 33( 97.1%) | 33(100.0%) | 66( 98.5%) |
| CPT B | 1( 2.9%) | .( . %) | 1( 1.5%) |
| **Baseline MELD Score** | | | |
| Mean (SE) | 9.12 (0.420) | 9.55 (0.343) | 9.33 (0.271) |
| Median | 9.00 | 9.00 | 9.00 |
| Range | ( 6.00, 14.00) | ( 7.00, 14.00) | ( 6.00, 14.00) |
| STD | 2.447 | 1.970 | 2.218 |
| **Baseline MELD Category** | | | |
| <10 | 19( 55.9%) | 17( 51.5%) | 36( 53.7%) |
| 10-15 | 15( 44.1%) | 16( 48.5%) | 31( 46.3%) |
| **IL28B genotype** | | | |
| CC | 3( 8.8%) | 7( 21.2%) | 10( 14.9%) |
| CT | 23( 67.6%) | 21( 63.6%) | 44( 65.7%) |
| TT | 8( 23.5%) | 5( 15.2%) | 13( 19.4%) |
| **Prior Treatment Category** | | | |
| Treatment-experienced | 31( 91.2%) | 29( 87.9%) | 60( 89.6%) |
| Treatment-naive | 3( 8.8%) | 4( 12.1%) | 7( 10.4%) |
| **Prior Response Category** | | | |
| n | 31 | 29 | 60 |
| Non-Responder | 17( 54.8%) | 17( 58.6%) | 34( 56.7%) |
| Relapse/Breakthrough | 14( 45.2%) | 12( 41.4%) | 26( 43.3%) |
| **Prior Treatment** | | | |
| n | 31 | 29 | 60 |
| Other | 2( 6.5%) | 3( 10.3%) | 5( 8.3%) |
| PEG + RBV | 22( 71.0%) | 20( 69.0%) | 42( 70.0%) |
| PI + PEG + RBV | 7( 22.6%) | 6( 20.7%) | 13( 21.7%) |
| **Baseline GFR** | | | |
| Mean (SE) | 65.27 (3.501) | 64.02 (3.551) | 64.65 (2.475) |
| Median | 65.49 | 60.78 | 63.56 |
| Range | (29.24, 123.5) | (27.79, 132.1) | (27.79, 132.1) |
| STD | 20.41 | 20.40 | 20.26 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Country | | | |
| AUS | 3( 8.8%) | 3( 9.1%) | 6( 9.0%) |
| AUT | 2( 5.9%) | 3( 9.1%) | 5( 7.5%) |
| BEL | 1( 2.9%) | 1( 3.0%) | 2( 3.0%) |
| CAN | 4( 11.8%) | 5( 15.2%) | 9( 13.4%) |
| CHE | 4( 11.8%) | 2( 6.1%) | 6( 9.0%) |
| DEU | .( . %) | 3( 9.1%) | 3( 4.5%) |
| ESP | 5( 14.7%) | 5( 15.2%) | 10( 14.9%) |
| FRA | 6( 17.6%) | 3( 9.1%) | 9( 13.4%) |
| GBR | 4( 11.8%) | 5( 15.2%) | 9( 13.4%) |
| ITA | 3( 8.8%) | 1( 3.0%) | 4( 6.0%) |
| NZL | 2( 5.9%) | 2( 6.1%) | 4( 6.0%) |
| Region | | | |
| Non-US | 34(100.0%) | 33(100.0%) | 67(100.0%) |

**Table 42:** Demographics and Baseline Characteristics of Group 5 in Study SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 22 | 23 | 45 |
| Gender | | | |
| F | 7( 31.8%) | 8( 34.8%) | 15( 33.3%) |
| M | 15( 68.2%) | 15( 65.2%) | 30( 66.7%) |
| Race | | | |
| WHITE | 21( 95.5%) | 21( 91.3%) | 42( 93.3%) |
| ASIAN | .( . %) | 1( 4.3%) | 1( 2.2%) |
| BLACK OR AFRICAN AMERICAN | .( . %) | 1( 4.3%) | 1( 2.2%) |
| OTHER | 1( 4.5%) | .( . %) | 1( 2.2%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 3( 13.6%) | 4( 17.4%) | 7( 15.6%) |
| NOT HISPANIC OR LATINO | 19( 86.4%) | 19( 82.6%) | 38( 84.4%) |
| Age (Year) | | | |
| Mean (SE) | 57.6 (1.71) | 59.8 (2.13) | 58.8 (1.37) |
| Median | 58.0 | 60.0 | 59.0 |
| Range | (41, 76) | (23, 74) | (23, 76) |
| STD | 8.033 | 10.20 | 9.166 |
| Age Category | | | |
| < 65 | 19( 86.4%) | 17( 73.9%) | 36( 80.0%) |
| >= 65 | 3( 13.6%) | 6( 26.1%) | 9( 20.0%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.13 (0.166) | 6.19 (0.177) | 6.16 (0.120) |
| Median | 6.21 | 6.37 | 6.23 |
| Range | ( 3.71, 7.12) | ( 3.40, 7.38) | ( 3.40, 7.38) |
| STD | 0.779 | 0.851 | 0.808 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 5( 22.7%) | 9( 39.1%) | 14( 31.1%) |
| >= 800,000 IU/mL | 17( 77.3%) | 14( 60.9%) | 31( 68.9%) |
| Baseline Genotype | | | |
| 1a | 11( 50.0%) | 13( 56.5%) | 24( 53.3%) |
| 1b | 9( 40.9%) | 7( 30.4%) | 16( 35.6%) |
| 4 | .( . %) | 3( 13.0%) | 3( 6.7%) |
| 4a/4c/4d | 2( 9.1%) | .( . %) | 2( 4.4%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 26.80 (1.063) | 26.58 (0.683) | 26.68 (0.619) |
| Median | 25.72 | 26.76 | 25.81 |
| Range | (20.88, 39.56) | (20.20, 32.79) | (20.20, 39.56) |
| STD | 4.987 | 3.276 | 4.153 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 16( 72.7%) | 20( 87.0%) | 36( 80.0%) |
| >= 30 kg/m2 | 6( 27.3%) | 3( 13.0%) | 9( 20.0%) |
| Baseline Cirrhosis Status | | | |
| Y | 22(100.0%) | 23(100.0%) | 45(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 71.32 (9.558) | 87.61 (11.85) | 79.64 (7.664) |
| Median | 60.00 | 79.00 | 66.00 |
| Range | (14.00, 208.0) | (12.00, 234.0) | (12.00, 234.0) |
| STD | 44.83 | 56.85 | 51.41 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 11( 50.0%) | 9( 39.1%) | 20( 44.4%) |
| > 1.5 x ULN | 11( 50.0%) | 14( 60.9%) | 25( 55.6%) |
| Baseline CPT Score | | | |
| Mean (SE) | 7.59 (0.215) | 7.65 (0.256) | 7.62 (0.166) |
| Median | 8.00 | 7.00 | 8.00 |
| Range | ( 5.00, 9.00) | ( 6.00, 11.00) | ( 5.00, 11.00) |
| STD | 1.008 | 1.229 | 1.114 |
| Baseline CPT Category | | | |
| CPT A | 3( 13.6%) | 2( 8.7%) | 5( 11.1%) |
| CPT B | 19( 86.4%) | 19( 82.6%) | 38( 84.4%) |
| CPT C | .( . %) | 2( 8.7%) | 2( 4.4%) |
| Baseline MELD Score | | | |
| Mean (SE) | 11.64 (0.695) | 11.57 (0.764) | 11.60 (0.512) |
| Median | 11.00 | 12.00 | 11.00 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Range | ( 6.00, 18.00) | ( 6.00, 19.00) | ( 6.00, 19.00) |
| STD | 3.259 | 3.666 | 3.434 |
| **Baseline MELD Category** | | | |
| <10 | 5( 22.7%) | 7( 30.4%) | 12( 26.7%) |
| 10-15 | 13( 59.1%) | 13( 56.5%) | 26( 57.8%) |
| 16-20 | 4( 18.2%) | 3( 13.0%) | 7( 15.6%) |
| **IL28B genotype** | | | |
| CC | 3( 13.6%) | 5( 21.7%) | 8( 17.8%) |
| CT | 12( 54.5%) | 11( 47.8%) | 23( 51.1%) |
| TT | 7( 31.8%) | 7( 30.4%) | 14( 31.1%) |
| **Prior Treatment Category** | | | |
| Treatment-experienced | 18( 81.8%) | 19( 82.6%) | 37( 82.2%) |
| Treatment-naive | 4( 18.2%) | 4( 17.4%) | 8( 17.8%) |
| **Prior Response Category** | | | |
| n | 18 | 19 | 37 |
| Non-Responder | 16( 88.9%) | 15( 78.9%) | 31( 83.8%) |
| Relapse/Breakthrough | 2( 11.1%) | 4( 21.1%) | 6( 16.2%) |
| **Prior Treatment** | | | |
| n | 18 | 19 | 37 |
| Other | 7( 38.9%) | 2( 10.5%) | 9( 24.3%) |
| PEG + RBV | 9( 50.0%) | 14( 73.7%) | 23( 62.2%) |
| PI + PEG + RBV | 2( 11.1%) | 3( 15.8%) | 5( 13.5%) |
| **Baseline GFR** | | | |
| Mean (SE) | 73.93 (5.042) | 65.85 (5.152) | 69.80 (3.617) |
| Median | 75.48 | 60.93 | 66.06 |
| Range | (30.36, 117.9) | (33.86, 123.9) | (30.36, 123.9) |
| STD | 23.65 | 24.71 | 24.27 |
| **Country** | | | |
| AUS | 2( 9.1%) | 2( 8.7%) | 4( 8.9%) |
| AUT | 1( 4.5%) | 2( 8.7%) | 3( 6.7%) |
| BEL | .( . %) | 2( 8.7%) | 2( 4.4%) |
| CAN | 4( 18.2%) | 5( 21.7%) | 9( 20.0%) |
| CHE | 2( 9.1%) | .( . %) | 2( 4.4%) |
| DEU | 1( 4.5%) | 1( 4.3%) | 2( 4.4%) |
| ESP | 3( 13.6%) | 4( 17.4%) | 7( 15.6%) |
| FRA | 3( 13.6%) | 3( 13.0%) | 6( 13.3%) |
| ITA | 3( 13.6%) | 3( 13.0%) | 6( 13.3%) |
| NLD | 1( 4.5%) | .( . %) | 1( 2.2%) |
| NZL | 2( 9.1%) | 1( 4.3%) | 3( 6.7%) |
| **Region** | | | |
| Non-US | 22(100.0%) | 23(100.0%) | 45(100.0%) |



Reference ID: 3884456

**Table 43:** Demographics and Baseline Characteristics of Group 6 in Study SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 3 | 5 | 8 |
| Gender | | | |
| F | 1( 33.3%) | .( . %) | 1( 12.5%) |
| M | 2( 66.7%) | 5(100.0%) | 7( 87.5%) |
| Race | | | |
| WHITE | 3(100.0%) | 5(100.0%) | 8(100.0%) |
| Ethnicity | | | |
| HISPANIC OR LATIN | 1( 33.3%) | 2( 40.0%) | 3( 37.5%) |
| NOT HISPANIC OR L | 2( 66.7%) | 3( 60.0%) | 5( 62.5%) |
| Age (Year) | | | |
| Mean (SE) | 62.0 (2.65) | 61.6 (4.13) | 61.8 (2.62) |
| Median | 63.0 | 62.0 | 62.50 |
| Range | (57, 66) | (52, 75) | (52, 75) |
| STD | 4.583 | 9.236 | 7.402 |
| Age Category | | | |
| < 65 | 2( 66.7%) | 3( 60.0%) | 5( 62.5%) |
| >= 65 | 1( 33.3%) | 2( 40.0%) | 3( 37.5%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.04 (0.283) | 6.47 (0.222) | 6.31 (0.181) |
| Median | 5.81 | 6.40 | 6.36 |
| Range | ( 5.70, 6.60) | ( 5.91, 7.27) | ( 5.70, 7.27) |
| STD | 0.490 | 0.497 | 0.511 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 2( 66.7%) | .( . %) | 2( 25.0%) |
| >= 800,000 IU/mL | 1( 33.3%) | 5(100.0%) | 6( 75.0%) |
| Baseline Genotype | | | |
| 1a | 1( 33.3%) | 1( 20.0%) | 2( 25.0%) |
| 1b | 1( 33.3%) | 4( 80.0%) | 5( 62.5%) |
| 4 | 1( 33.3%) | .( . %) | 1( 12.5%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 26.20 (0.332) | 25.06 (2.710) | 25.49 (1.637) |
| Median | 26.53 | 21.97 | 26.03 |
| Range | (25.54, 26.53) | (20.21, 34.38) | (20.21, 34.38) |
| STD | 0.575 | 6.060 | 4.629 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 3(100.0%) | 4( 80.0%) | 7( 87.5%) |
| >= 30 kg/m2 | .( . %) | 1( 20.0%) | 1( 12.5%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline Cirrhosis Status | | | |
| Y | 3(100.0%) | 5(100.0%) | 8(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 59.00 (8.000) | 97.00 (31.59) | 82.75 (20.29) |
| Median | 51.00 | 55.00 | 53.00 |
| Range | (51.00, 75.00) | (42.00, 201.0) | (42.00, 201.0) |
| STD | 13.86 | 70.63 | 57.38 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 2( 66.7%) | 2( 40.0%) | 4( 50.0%) |
| > 1.5 x ULN | 1( 33.3%) | 3( 60.0%) | 4( 50.0%) |
| Baseline CPT Score | | | |
| Mean (SE) | 11.67 (0.333) | 9.80 (0.200) | 10.50 (0.378) |
| Median | 12.00 | 10.00 | 10.00 |
| Range | (11.00, 12.00) | ( 9.00, 10.00) | ( 9.00, 12.00) |
| STD | 0.577 | 0.447 | 1.069 |
| Baseline CPT Category | | | |
| CPT B | .( . %) | 1( 20.0%) | 1( 12.5%) |
| CPT C | 3(100.0%) | 4( 80.0%) | 7( 87.5%) |
| Baseline MELD Score | | | |
| Mean (SE) | 16.33 (2.667) | 14.40 (0.748) | 15.13 (1.043) |
| Median | 19.00 | 14.00 | 14.50 |
| Range | (11.00, 19.00) | (13.00, 17.00) | (11.00, 19.00) |
| STD | 4.619 | 1.673 | 2.949 |
| Baseline MELD Category | | | |
| 10-15 | 1( 33.3%) | 4( 80.0%) | 5( 62.5%) |
| 16-20 | 2( 66.7%) | 1( 20.0%) | 3( 37.5%) |
| IL28B genotype | | | |
| CC | .( . %) | 3( 60.0%) | 3( 37.5%) |
| CT | 2( 66.7%) | 2( 40.0%) | 4( 50.0%) |
| TT | 1( 33.3%) | .( . %) | 1( 12.5%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 2( 66.7%) | 5(100.0%) | 7( 87.5%) |
| Treatment-naive | 1( 33.3%) | .( . %) | 1( 12.5%) |
| Prior Response Category | | | |
| n | 2 | 5 | 7 |
| Non-Responder | 1( 50.0%) | 2( 40.0%) | 3( 42.9%) |
| Relapse/Breakthrough | 1( 50.0%) | 3( 60.0%) | 4( 57.1%) |
| Prior Treatment | | | |
| n | 2 | 5 | 7 |
| Other | .( . %) | 2( 40.0%) | 2( 28.6%) |
| PEG + RBV | 2(100.0%) | 3( 60.0%) | 5( 71.4%) |
| Baseline GFR | | | |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Mean (SE) | 85.93 (12.82) | 60.70 (6.915) | 70.16 (7.484) |
| Median | 97.05 | 50.93 | 66.97 |
| Range | (60.35, 100.4) | (47.45, 81.07) | (47.45, 100.4) |
| STD | 22.21 | 15.46 | 21.17 |
| Country | | | |
| AUS | .( . %) | 1( 20.0%) | 1( 12.5%) |
| ESP | 1( 33.3%) | 2( 40.0%) | 3( 37.5%) |
| GBR | 1( 33.3%) | .( . %) | 1( 12.5%) |
| ITA | 1( 33.3%) | 2( 40.0%) | 3( 37.5%) |
| Region | | | |
| Non-US | 3(100.0%) | 5(100.0%) | 8(100.0%) |

**Table 44:** Demographics and Baseline Characteristics of Group 7 in Study SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 3 | 2 | 5 |
| Gender | | | |
| F | 1( 33.3%) | 1( 50.0%) | 2( 40.0%) |
| M | 2( 66.7%) | 1( 50.0%) | 3( 60.0%) |
| Race | | | |
| WHITE | 2( 66.7%) | 1( 50.0%) | 3( 60.0%) |
| ASIAN | 1( 33.3%) | 1( 50.0%) | 2( 40.0%) |
| Ethnicity | | | |
| NOT HISPANIC OR LATINO | 3(100.0%) | 2(100.0%) | 5(100.0%) |
| Age (Year) | | | |
| Mean (SE) | 58.0 (1.53) | 56.0 (2.00) | 57.2 (1.16) |
| Median | 57.0 | 56.0 | 57.0 |
| Range | (56, 61) | (54, 58) | (54, 61) |
| STD | 2.646 | 2.828 | 2.588 |
| Age Category | | | |
| < 65 | 3(100.0%) | 2(100.0%) | 5(100.0%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 7.31 (0.419) | 6.04 (0.288) | 6.80 (0.397) |
| Median | 7.39 | 6.04 | 6.55 |
| Range | ( 6.55, 7.99) | ( 5.75, 6.33) | ( 5.75, 7.99) |
| STD | 0.725 | 0.407 | 0.887 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | .( . %) | 1( 50.0%) | 1( 20.0%) |
| >= 800,000 IU/mL | 3(100.0%) | 1( 50.0%) | 4( 80.0%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline Genotype | | | |
| 1a | 2( 66.7%) | 2(100.0%) | 4( 80.0%) |
| 1b | 1( 33.3%) | .( . %) | 1( 20.0%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 22.36 (2.409) | 24.50 (0.613) | 23.22 (1.433) |
| Median | 24.47 | 24.50 | 24.47 |
| Range | (17.56, 25.06) | (23.89, 25.12) | (17.56, 25.12) |
| STD | 4.173 | 0.867 | 3.205 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 3(100.0%) | 2(100.0%) | 5(100.0%) |
| Baseline Cirrhosis Status | | | |
| N | 3(100.0%) | 2(100.0%) | 5(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 154.0 (42.45) | 164.5 (27.50) | 158.2 (24.96) |
| Median | 180.0 | 164.5 | 180.0 |
| Range | (71.00, 211.0) | (137.0, 192.0) | (71.00, 211.0) |
| STD | 73.53 | 38.89 | 55.81 |
| Baseline ALT Category | | | |
| > 1.5 x ULN | 3(100.0%) | 2(100.0%) | 5(100.0%) |
| Baseline CPT Score | | | |
| Mean (SE) | 8.00 (0.000) | 8.00 (2.000) | 8.00 (0.632) |
| Median | 8.00 | 8.00 | 8.00 |
| Range | ( 8.00, 8.00) | ( 6.00, 10.00) | ( 6.00, 10.00) |
| STD | 0.000 | 2.828 | 1.414 |
| Baseline CPT Category | | | |
| CPT A | .( . %) | 1( 50.0%) | 1( 20.0%) |
| CPT B | 3(100.0%) | .( . %) | 3( 60.0%) |
| CPT C | .( . %) | 1( 50.0%) | 1( 20.0%) |
| Baseline MELD Score | | | |
| Mean (SE) | 16.00 (1.732) | 15.00 (6.000) | 15.60 (2.135) |
| Median | 16.00 | 15.00 | 16.00 |
| Range | (13.00, 19.00) | ( 9.00, 21.00) | ( 9.00, 21.00) |
| STD | 3.000 | 8.485 | 4.775 |
| Baseline MELD Category | | | |
| <10 | .( . %) | 1( 50.0%) | 1( 20.0%) |
| 10-15 | 1( 33.3%) | .( . %) | 1( 20.0%) |
| 16-20 | 2( 66.7%) | .( . %) | 2( 40.0%) |
| 21-25 | .( . %) | 1( 50.0%) | 1( 20.0%) |
| IL28B genotype | | | |
| CC | .( . %) | 1( 50.0%) | 1( 20.0%) |
| CT | 3(100.0%) | 1( 50.0%) | 4( 80.0%) |



Reference ID: 3884456

```
Prior Treatment Category
  Treatment-experienced   2( 66.7%)        2(100.0%)        4( 80.0%)
  Treatment-naive         1( 33.3%)        .(    . %)       1( 20.0%)

Prior Response Category
  n                                 2                 2                 4
  Non-Responder           2(100.0%)        1( 50.0%)        3( 75.0%)
  Relapse/Breakthrough    .(    . %)       1( 50.0%)        1( 25.0%)

Prior Treatment
  n                                 2                 2                 4
  PEG + RBV               2(100.0%)        2(100.0%)        4(100.0%)

Baseline GFR
  Mean (SE)             87.47 (3.895)    88.97 (13.71)    88.07 (4.847)
  Median                        88.09            88.97            88.09
  Range                (80.44,  93.89)  (75.26,  102.7)  (75.26,  102.7)
  STD                           6.746            19.39            10.84

Country
  AUS                     .(    . %)       1( 50.0%)        1( 20.0%)
  CAN                     .(    . %)       1( 50.0%)        1( 20.0%)
  FRA                     1( 33.3%)        .(    . %)       1( 20.0%)
  NZL                     2( 66.7%)        .(    . %)       2( 40.0%)

Region
  Non-US                  3(100.0%)        2(100.0%)        5(100.0%)
-----------------------------------------------------------------------
```

**Table 45:** The List of Subjects who had Different Planned and Actual Treatment Group for Study SOLAR-2 (FAS)

| | USUBJID | TRT01A | TRT01P | FASFL | SVR12 | SVR4 | BALT | group | trt | Bcpt | Bmeld | CPTCat | MeldCat |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | GS-US-337-0124-1305-76115 | Cohort A, Group 2 - 12 Weeks of Treatment | Cohort A, Group 1 - 12 Weeks of Treatment | Y | Y | Y | 30 | G2 | T12WK | 9 | 15 | CPT B | 10-15 |
| 2 | GS-US-337-0124-1222-76153 | Cohort A, Group 2 - 24 Weeks of Treatment | Cohort A, Group 1 - 24 Weeks of Treatment | Y | Y | Y | 59 | G2 | T24WK | 10 | 13 | CPT C | 10-15 |
| 3 | GS-US-337-0124-8632-76149 | Cohort A, Group 2 - 24 Weeks of Treatment | Cohort A, Group 1 - 24 Weeks of Treatment | Y | | | 51 | G2 | T24WK | 11 | 17 | CPT C | 16-20 |
| 4 | GS-US-337-0124-2456-76238 | Cohort A, Group 1 - 24 Weeks of Treatment | Cohort A, Group 2 - 24 Weeks of Treatment | Y | Y | Y | 34 | G1 | T24WK | 11 | 14 | CPT C | 10-15 |
| 5 | GS-US-337-0124-1069-76396 | Cohort B, Group 4 - 12 Weeks of Treatment | Cohort B, Group 3 - 12 Weeks of Treatment | Y | Y | Y | 145 | G4 | T12WK | 6 | 6 | CPT A | <10 |
| 6 | GS-US-337-0124-1069-76301 | Cohort B, Group 4 - 24 Weeks of Treatment | Cohort B, Group 3 - 24 Weeks of Treatment | Y | Y | Y | 163 | G4 | T24WK | 6 | 12 | CPT A | 10-15 |
| 7 | GS-US-337-0124-1253-76374 | Cohort B, Group 4 - 24 Weeks of Treatment | Cohort B, Group 3 - 24 Weeks of Treatment | Y | Y | Y | 57 | G4 | T24WK | 5 | 9 | CPT A | <10 |
| 8 | GS-US-337-0124-0676-76410 | Cohort B, Group 3 - 12 Weeks of Treatment | Cohort B, Group 4 - 12 Weeks of Treatment | Y | Y | Y | 72 | G3 | T12WK | 5 | 8 | CPT A | <10 |
| 9 | GS-US-337-0124-1043-76408 | Cohort B, Group 5 - 12 Weeks of Treatment | Cohort B, Group 4 - 12 Weeks of Treatment | Y | Y | Y | 86 | G5 | T12WK | 6 | 9 | CPT A | <10 |
| 10 | GS-US-337-0124-0676-76407 | Cohort B, Group 3 - 24 Weeks of Treatment | Cohort B, Group 4 - 24 Weeks of Treatment | Y | Y | Y | 348 | G3 | T24WK | 6 | 15 | CPT A | 10-15 |
| 11 | GS-US-337-0124-0454-76532 | Cohort B, Group 4 - 12 Weeks of Treatment | Cohort B, Group 5 - 12 Weeks of Treatment | Y | N | N | 114 | G4 | T12WK | 6 | 11 | CPT A | 10-15 |
| 12 | GS-US-337-0124-0676-76505 | Cohort B, Group 4 - 12 Weeks of Treatment | Cohort B, Group 5 - 12 Weeks of Treatment | Y | Y | Y | 258 | G4 | T12WK | 6 | 11 | CPT A | 10-15 |
| 13 | GS-US-337-0124-8632-76524 | Cohort B, Group 4 - 12 Weeks of Treatment | Cohort B, Group 5 - 12 Weeks of Treatment | Y | Y | Y | 161 | G4 | T12WK | 6 | 14 | CPT A | 10-15 |
| 14 | GS-US-337-0124-0480-76534 | Cohort B, Group 6 - 24 Weeks of Treatment | Cohort B, Group 5 - 24 Weeks of Treatment | Y | Y | Y | 140 | G6 | T24WK | 9 | 13 | CPT B | 10-15 |
| 15 | GS-US-337-0124-0676-76530 | Cohort B, Group 4 - 24 Weeks of Treatment | Cohort B, Group 5 - 24 Weeks of Treatment | Y | Y | Y | 40 | G4 | T24WK | 6 | 14 | CPT A | 10-15 |
| 16 | GS-US-337-0124-1222-76521 | Cohort B, Group 6 - 24 Weeks of Treatment | Cohort B, Group 5 - 24 Weeks of Treatment | Y | Y | Y | 47 | G6 | T24WK | 10 | 14 | CPT C | 10-15 |
| 17 | GS-US-337-0124-1043-76602 | Cohort B, Group 5 - 12 Weeks of Treatment | Cohort B, Group 6 - 12 Weeks of Treatment | Y | Y | Y | 52 | G5 | T12WK | 8 | 10 | CPT B | 10-15 |
| 18 | GS-US-337-0124-0676-76604 | Cohort B, Group 5 - 24 Weeks of Treatment | Cohort B, Group 6 - 24 Weeks of Treatment | Y | Y | Y | 47 | G5 | T24WK | 9 | 12 | CPT B | 10-15 |
| 19 | GS-US-337-0124-7926-76605 | Cohort B, Group 5 - 24 Weeks of Treatment | Cohort B, Group 6 - 24 Weeks of Treatment | Y | Y | Y | 41 | G5 | T24WK | 11 | 18 | CPT C | 16-20 |
| 20 | GS-US-337-0124-2054-76707 | Cohort B, Group 3 - 12 Weeks of Treatment | Cohort B, Group 7 - 12 Weeks of Treatment | Y | N | N | 194 | G3 | T12WK | 9 | 19 | CPT B | 16-20 |



Reference ID: 3884456

**Table 46:** The List of Subjects who had Liver Transplant during the Study for SOLAR-2 (FAS)

**Table 9-3. GS-US-337-0124: pTVR12 Outcomes for Subjects Who Underwent Liver Transplantation During the Study (Full Analysis Set with HCV RNA < LLOQ at Last Measurement Prior to Liver Transplantation Analysis Set [Last Observed HCV RNA Prior to Transplantation < LLOQ])**

| Subject Number | Liver Disease Status (Group) | Study Treatment | Date of Last Dose of Study Drug (Study Day) | Date of Transplantation | Outcome | |
|---|---|---|---|---|---|---|
| 0452-76215 | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 12 Weeks | | (b) (6) | pTVR12 | |
| 0480-76236 | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 12 Weeks | | | pTVR12 | |
| 0480-76237 | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 12 Weeks | | | pTVR12 | |
| 0957-76227 | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 12 Weeks | | | pTVR12 | SVR12=Y |
| 1119-76247 | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 12 Weeks | | | pTVR12 | |
| 1474-76133 | CPT B Cirrhosis (Group 1) | LDV/SOF+RBV 12 Weeks | | | pTVR12 | SVR12=Y |
| 1759-76125 | CPT B Cirrhosis (Group 1) | LDV/SOF+RBV 24 Weeks | | | pTVR12 | |
| 4472-76141 | CPT B Cirrhosis (Group 1) | LDV/SOF+RBV 24 Weeks | | | pTVR12 | SVR8=Y, SVR12="" |
| 7926-76522 | CPT B Cirrhosis (Group 5) | LDV/SOF+RBV 24 Weeks | | | NA[a] | SVR12=Y |
| 8632-76149 | CPT C Cirrhosis (Group 2) | LDV/SOF+RBV 24 Weeks | | | pTVR12 | |

Source: Table 9-3 in CSR of SOLAR-2 with some additional information added.

**Table 47:** Primary Efficacy Results (SVR12) by Group for SOLAR-2 (Efficacy Analysis Set)

| Cohort | Group | T12WK | T24WK |
|---|---|---|---|
| A (pre-transplant) | G1: CPT B | 84.6% (22/26) | 96.0% (24/25) |
| | G2: CPT C | 81.0% (17/21) | 76.0% (19/25 |
| B (Post-transplant) | G3: F0-F3 Fibrosis | 94.2% (49/52) | 100% (49/49) |
| | G4: CPT A | 97.1% (33/34) | 97.0% (32/33) |
| | G5: CPT B | 95.5% (21/22) | 100% (23/23) |
| | G6: CPT C | 33.3% (1/3) | 80.0% (4/5) |
| | G7: FCH | 100% (3/3) | 100 (2/2) |

**Table 48:** SVR12 Rate of by Group Combination (Pre vs. Post) for SOLAR-2 (Efficacy Analysis Set)

| Transplant Status | Cirrhosis Status | T12WK | T24WK |
|---|---|---|---|
| Pre-transplanted (CPT B / C) | Decompensated (G1+G2) | 83.0% (39/47) | 86.0% (43/50) |
| Post-transplanted (CPT B / C) | Decompensated (G5+G6) | 88.0% (22/25) | 96.4% (27/28) |
| Post-transplanted (CPT A) | Compensated (G3+G4) | 95.4% (82/86) | 98.8% (81/82) |

**Table 49:** SVR12 Rate of by Group Combination (CPT Category) for SOLAR-2 (Efficacy Analysis Set)

| CPT Category | Cirrhosis Status | T12WK | T24WK |
|---|---|---|---|
| CPT B | Decompensated (G1+G5) | 89.6% (43/48) | 97.9% (47/48) |
| CPT C | Decompensated (G2+G6) | 75.0% (18/24) | 76.7% (23/30) |
| CPT B/C | Decompensated (G1+G5+G2+G6) | 84.7% (61/72) | 89.7% (70/78) |



Reference ID: 3884456

**Table 50:** Demographics and Baseline Characteristics of Studies SOLAR-1 and SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 336 | 334 | 670 |
| Gender | | | |
| F | 79( 23.5%) | 76( 22.8%) | 155( 23.1%) |
| M | 257( 76.5%) | 258( 77.2%) | 515( 76.9%) |
| Race | | | |
| WHITE | 307( 91.4%) | 306( 91.6%) | 613( 91.5%) |
| BLACK OR AFRICAN AMERICAN | 19( 5.7%) | 16( 4.8%) | 35( 5.2%) |
| AMERICAN INDIAN OR ALASKA NATIVE | 2( 0.6%) | 1( 0.3%) | 3( 0.4%) |
| NATIVE HAWAIIAN OR PACIFIC ISLANDER | 2( 0.6%) | .( . %) | 2( 0.3%) |
| ASIAN | 1( 0.3%) | 7( 2.1%) | 8( 1.2%) |
| OTHER | 5( 1.5%) | 4( 1.2%) | 9( 1.3%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 42( 12.5%) | 53( 15.9%) | 95( 14.2%) |
| NOT HISPANIC OR LATINO | 294( 87.5%) | 281( 84.1%) | 575( 85.8%) |
| Age (Year) | | | |
| Mean (SE) | 58.00 (0.408) | 58.78 (0.430) | 58.39 (0.297) |
| Median | 59.00 | 59.00 | 59.00 |
| Range | (27.00, 78.00) | (21.00, 81.00) | (21.00, 81.00) |
| STD | 7.472 | 7.868 | 7.676 |
| Age Category | | | |
| < 65 | 283( 84.2%) | 271( 81.1%) | 554( 82.7%) |
| >= 65 | 53( 15.8%) | 63( 18.9%) | 116( 17.3%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.17 (0.039) | 6.23 (0.040) | 6.20 (0.028) |
| Median | 6.25 | 6.34 | 6.31 |
| Range | ( 3.71, 7.99) | ( 2.40, 7.83) | ( 2.40, 7.99) |
| STD | 0.708 | 0.733 | 0.721 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 108( 32.1%) | 96( 28.7%) | 204( 30.4%) |
| >= 800,000 IU/mL | 228( 67.9%) | 238( 71.3%) | 466( 69.6%) |
| Baseline Genotype | | | |
| 1a | 199( 59.2%) | 202( 60.5%) | 401( 59.9%) |
| 1b | 115( 34.2%) | 112( 33.5%) | 227( 33.9%) |
| 4 | 10( 3.0%) | 10( 3.0%) | 20( 3.0%) |
| 4a | 1( 0.3%) | .( . %) | 1( 0.1%) |
| 4a/4c/4d | 8( 2.4%) | 9( 2.7%) | 17( 2.5%) |
| 4e | .( . %) | 1( 0.3%) | 1( 0.1%) |
| 4h | 2( 0.6%) | .( . %) | 2( 0.3%) |
| 4r | 1( 0.3%) | .( . %) | 1( 0.1%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 28.37 (0.297) | 27.35 (0.239) | 27.86 (0.192) |
| Median | 27.55 | 26.82 | 27.17 |
| Range | (17.56, 48.53) | (17.59, 45.23) | (17.56, 48.53) |
| STD | 5.453 | 4.369 | 4.965 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 222( 66.1%) | 259( 77.5%) | 481( 71.8%) |
| >= 30 kg/m2 | 114( 33.9%) | 75( 22.5%) | 189( 28.2%) |
| Baseline Cirrhosis Status | | | |
| N | 114( 33.9%) | 109( 32.6%) | 223( 33.3%) |
| Y | 222( 66.1%) | 225( 67.4%) | 447( 66.7%) |
| Baseline ALT | | | |
| Mean (SE) | 80.22 (2.932) | 85.79 (3.621) | 83.00 (2.329) |
| Median | 64.50 | 67.00 | 65.00 |
| Range | (14.00, 271.0) | (12.00, 570.0) | (12.00, 570.0) |
| STD | 53.74 | 66.17 | 60.28 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 155( 46.1%) | 153( 45.8%) | 308( 46.0%) |
| > 1.5 x ULN | 181( 53.9%) | 181( 54.2%) | 362( 54.0%) |
| Baseline CPT Score | | | |
| n | 334 | 332 | 666 |
| Mean (SE) | 7.07 (0.111) | 7.06 (0.113) | 7.07 (0.079) |
| Median | 7.00 | 7.00 | 7.00 |
| Range | ( 5.00, 12.00) | ( 5.00, 12.00) | ( 5.00, 12.00) |
| STD | 2.029 | 2.058 | 2.042 |
| Baseline CPT Category | | | |
| n | 334 | 332 | 666 |
| CPT A | 161( 48.2%) | 162( 48.8%) | 323( 48.5%) |
| CPT B | 124( 37.1%) | 111( 33.4%) | 235( 35.3%) |
| CPT C | 49( 14.7%) | 59( 17.8%) | 108( 16.2%) |
| Baseline MELD Score | | | |
| n | 333 | 331 | 664 |
| Mean (SE) | 11.34 (0.200) | 11.16 (0.203) | 11.25 (0.142) |
| Median | 11.00 | 11.00 | 11.00 |
| Range | ( 6.00, 24.00) | ( 6.00, 24.00) | ( 6.00, 24.00) |
| STD | 3.648 | 3.691 | 3.668 |
| Baseline MELD Category | | | |
| n | 336 | 334 | 670 |
| <10 | 119( 35.4%) | 127( 38.0%) | 246( 36.7%) |
| 10-15 | 168( 50.0%) | 161( 48.2%) | 329( 49.1%) |
| 16-20 | 44( 13.1%) | 41( 12.3%) | 85( 12.7%) |
| 21-25 | 5( 1.5%) | 5( 1.5%) | 10( 1.5%) |
| IL28B genotype | | | |
| CC | 61( 18.2%) | 68( 20.4%) | 129( 19.3%) |
| CT | 194( 57.7%) | 183( 54.8%) | 377( 56.3%) |
| TT | 81( 24.1%) | 83( 24.9%) | 164( 24.5%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Prior Treatment Category | | | |
| Treatment-experienced | 256( 76.2%) | 269( 80.5%) | 525( 78.4%) |
| Treatment-naive | 80( 23.8%) | 65( 19.5%) | 145( 21.6%) |
| Prior Response Category | | | |
| n | 254 | 267 | 521 |
| Non-Responder | 175( 68.9%) | 174( 65.2%) | 349( 67.0%) |
| Relapse/Breakthrough | 79( 31.1%) | 93( 34.8%) | 172( 33.0%) |
| Prior Treatment | | | |
| n | 256 | 269 | 525 |
| Other | 27( 10.5%) | 20( 7.4%) | 47( 9.0%) |
| PEG + RBV | 177( 69.1%) | 201( 74.7%) | 378( 72.0%) |
| PI + PEG + RBV | 52( 20.3%) | 48( 17.8%) | 100( 19.0%) |
| Baseline GFR | | | |
| n | 335 | 333 | 668 |
| Mean (SE) | 72.97 (1.417) | 74.11 (1.434) | 73.54 (1.007) |
| Median | 68.44 | 69.56 | 69.20 |
| Range | (20.44, 189.9) | (26.76, 223.6) | (20.44, 223.6) |
| STD | 25.93 | 26.17 | 26.04 |
| Country | | | |
| AUS | 13( 3.9%) | 14( 4.2%) | 27( 4.0%) |
| AUT | 14( 4.2%) | 9( 2.7%) | 23( 3.4%) |
| BEL | 8( 2.4%) | 8( 2.4%) | 16( 2.4%) |
| CAN | 26( 7.7%) | 23( 6.9%) | 49( 7.3%) |
| CHE | 12( 3.6%) | 11( 3.3%) | 23( 3.4%) |
| DEU | 12( 3.6%) | 16( 4.8%) | 28( 4.2%) |
| ESP | 21( 6.3%) | 31( 9.3%) | 52( 7.8%) |
| FRA | 16( 4.8%) | 16( 4.8%) | 32( 4.8%) |
| GBR | 18( 5.4%) | 18( 5.4%) | 36( 5.4%) |
| ITA | 13( 3.9%) | 10( 3.0%) | 23( 3.4%) |
| NLD | 4( 1.2%) | 4( 1.2%) | 8( 1.2%) |
| NZL | 10( 3.0%) | 6( 1.8%) | 16( 2.4%) |
| USA | 169( 50.3%) | 168( 50.3%) | 337( 50.3%) |
| Region | | | |
| No | 167( 49.7%) | 166( 49.7%) | 333( 49.7%) |
| US | 169( 50.3%) | 168( 50.3%) | 337( 50.3%) |

**Table 51:** Demographics and Baseline Characteristics of Group 1 in Studies SOLAR-1 and SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 58 | 57 | 115 |
| Gender | | | |
| F | 13( 22.4%) | 20( 35.1%) | 33( 28.7%) |
| M | 45( 77.6%) | 37( 64.9%) | 82( 71.3%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Race | | | |
| WHITE | 54( 93.1%) | 54( 94.7%) | 108( 93.9%) |
| BLACK OR AFRICAN AMERICAN | 2( 3.4%) | 3( 5.3%) | 5( 4.3%) |
| NATIVE HAWAIIAN OR PACIFIC ISLANDER | 1( 1.7%) | .( . %) | 1( 0.9%) |
| OTHER | 1( 1.7%) | .( . %) | 1( 0.9%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 10( 17.2%) | 9( 15.8%) | 19( 16.5%) |
| NOT HISPANIC OR LATINO | 48( 82.8%) | 48( 84.2%) | 96( 83.5%) |
| Age (Year) | | | |
| Mean (SE) | 55.9 (1.24) | 57.1 (1.00) | 56.5 (0.80) |
| Median | 58 | 58 | 58 |
| Range | (27, 71) | (35, 74) | (27, 74) |
| STD | 9.44 | 7.55 | 8.54 |
| Age Category | | | |
| < 65 | 52( 89.7%) | 51( 89.5%) | 103( 89.6%) |
| >= 65 | 6( 10.3%) | 6( 10.5%) | 12( 10.4%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 5.94 (0.078) | 5.87 (0.093) | 5.91 (0.061) |
| Median | 6.01 | 5.95 | 5.99 |
| Range | ( 4.28, 6.94) | ( 3.24, 7.12) | ( 3.24, 7.12) |
| STD | 0.597 | 0.701 | 0.649 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 25( 43.1%) | 25( 43.9%) | 50( 43.5%) |
| >= 800,000 IU/mL | 33( 56.9%) | 32( 56.1%) | 65( 56.5%) |
| Baseline Genotype | | | |
| 1a | 32( 55.2%) | 34( 59.6%) | 66( 57.4%) |
| 1b | 22( 37.9%) | 20( 35.1%) | 42( 36.5%) |
| 4 | .( . %) | 2( 3.5%) | 2( 1.7%) |
| 4a | 1( 1.7%) | .( . %) | 1( 0.9%) |
| 4a/4c/4d | 2( 3.4%) | 1( 1.8%) | 3( 2.6%) |
| 4r | 1( 1.7%) | .( . %) | 1( 0.9%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 28.35 (0.648) | 28.30 (0.599) | 28.33 (0.439) |
| Median | 27.69 | 28.55 | 27.90 |
| Range | (20.22, 47.00) | (20.03, 45.23) | (20.03, 47.00) |
| STD | 4.933 | 4.519 | 4.712 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 43( 74.1%) | 42( 73.7%) | 85( 73.9%) |
| >= 30 kg/m2 | 15( 25.9%) | 15( 26.3%) | 30( 26.1%) |
| Baseline Cirrhosis Status | | | |
| Y | 58(100.0%) | 57(100.0%) | 115(100.0%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline ALT | | | |
| Mean (SE) | 71.88 (4.631) | 77.23 (5.109) | 74.53 (3.439) |
| Median | 63.00 | 70.00 | 66.00 |
| Range | (30.00, 221.0) | (14.00, 184.0) | (14.00, 221.0) |
| STD | 35.27 | 38.57 | 36.88 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 27( 46.6%) | 21( 36.8%) | 48( 41.7%) |
| > 1.5 x ULN | 31( 53.4%) | 36( 63.2%) | 67( 58.3%) |
| Baseline CPT Score | | | |
| n | 56 | 56 | 112 |
| Mean (SE) | 8.13 (0.108) | 7.98 (0.126) | 8.05 (0.083) |
| Median | 8.00 | 8.00 | 8.00 |
| Range | ( 7.00, 10.00) | ( 6.00, 11.00) | ( 6.00, 11.00) |
| STD | 0.810 | 0.944 | 0.879 |
| Baseline CPT Category | | | |
| n | 56 | 56 | 112 |
| CPT A | .( . %) | 1( 1.8%) | 1( 0.9%) |
| CPT B | 52( 92.9%) | 53( 94.6%) | 105( 93.8%) |
| CPT C | 4( 7.1%) | 2( 3.6%) | 6( 5.4%) |
| Baseline MELD Score | | | |
| n | 56 | 56 | 112 |
| Mean (SE) | 12.21 (0.317) | 11.63 (0.392) | 11.92 (0.252) |
| Median | 12.00 | 11.00 | 12.00 |
| Range | ( 7.00, 17.00) | ( 6.00, 18.00) | ( 6.00, 18.00) |
| STD | 2.372 | 2.933 | 2.672 |
| Baseline MELD Category | | | |
| <10 | 9( 15.5%) | 14( 24.6%) | 23( 20.0%) |
| 10-15 | 42( 72.4%) | 34( 59.6%) | 76( 66.1%) |
| 16-20 | 7( 12.1%) | 9( 15.8%) | 16( 13.9%) |
| IL28B genotype | | | |
| CC | 10( 17.2%) | 14( 24.6%) | 24( 20.9%) |
| CT | 38( 65.5%) | 28( 49.1%) | 66( 57.4%) |
| TT | 10( 17.2%) | 15( 26.3%) | 25( 21.7%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 47( 81.0%) | 43( 75.4%) | 90( 78.3%) |
| Treatment-naive | 11( 19.0%) | 14( 24.6%) | 25( 21.7%) |
| Prior Response Category | | | |
| n | 46 | 42 | 88 |
| Non-Responder | 35( 76.1%) | 27( 64.3%) | 62( 70.5%) |
| Relapse/Breakthrough | 11( 23.9%) | 15( 35.7%) | 26( 29.5%) |
| Prior Treatment | | | |
| n | 47 | 43 | 90 |
| Other | 5( 10.6%) | 1( 2.3%) | 6( 6.7%) |
| PEG + RBV | 29( 61.7%) | 30( 69.8%) | 59( 65.6%) |
| PI + PEG + RBV | 13( 27.7%) | 12( 27.9%) | 25( 27.8%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline GFR | | | |
| Mean (SE) | 98.10 (4.606) | 89.55 (3.762) | 93.86 (2.992) |
| Median | 93.15 | 84.27 | 90.52 |
| Range | (33.93, 189.9) | (37.40, 164.2) | (33.93, 189.9) |
| STD | 35.08 | 28.40 | 32.09 |
| Country | | | |
| AUS | 1( 1.7%) | 1( 1.8%) | 2( 1.7%) |
| AUT | 2( 3.4%) | 2( 3.5%) | 4( 3.5%) |
| BEL | 1( 1.7%) | 2( 3.5%) | 3( 2.6%) |
| CAN | 6( 10.3%) | 5( 8.8%) | 11( 9.6%) |
| CHE | 1( 1.7%) | 4( 7.0%) | 5( 4.3%) |
| DEU | 2( 3.4%) | 4( 7.0%) | 6( 5.2%) |
| ESP | 6( 10.3%) | 5( 8.8%) | 11( 9.6%) |
| FRA | 1( 1.7%) | 1( 1.8%) | 2( 1.7%) |
| GBR | 5( 8.6%) | 3( 5.3%) | 8( 7.0%) |
| ITA | 2( 3.4%) | 1( 1.8%) | 3( 2.6%) |
| NZL | 1( 1.7%) | .( . %) | 1( 0.9%) |
| USA | 30( 51.7%) | 29( 50.9%) | 59( 51.3%) |
| Region | | | |
| Non-US | 28( 48.3%) | 28( 49.1%) | 56( 48.7%) |
| US | 30( 51.7%) | 29( 50.9%) | 59( 51.3%) |

**Table 52:** Demographics and Baseline Characteristics of Group 2 in Studies SOLAR-1 and SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 48 | 52 | 100 |
| Gender | | | |
| F | 19( 39.6%) | 14( 26.9%) | 33( 33.0%) |
| M | 29( 60.4%) | 38( 73.1%) | 67( 67.0%) |
| Race | | | |
| WHITE | 44( 91.7%) | 49( 94.2%) | 93( 93.0%) |
| BLACK OR AFRICAN AMERICAN | 3( 6.3%) | 2( 3.8%) | 5( 5.0%) |
| OTHER | 1( 2.1%) | 1( 1.9%) | 2( 2.0%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 5( 10.4%) | 12( 23.1%) | 17( 17.0%) |
| NOT HISPANIC OR LATINO | 43( 89.6%) | 40( 76.9%) | 83( 83.0%) |
| Age (Year) | | | |
| Mean (SE) | 57.6 (1.05) | 56.5 (1.16) | 57.0 (0.78) |
| Median | 58 | 57 | 57.5 |
| Range | (39, 74) | (40, 79) | (39, 79) |
| STD | 7.249 | 8.382 | 7.838 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Age Category | | | |
| < 65 | 42( 87.5%) | 45( 86.5%) | 87( 87.0%) |
| >= 65 | 6( 12.5%) | 7( 13.5%) | 13( 13.0%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 5.61 (0.086) | 5.74 (0.081) | 5.68 (0.059) |
| Median | 5.66 | 5.75 | 5.70 |
| Range | ( 4.07, 6.77) | ( 3.67, 6.88) | ( 3.67, 6.88) |
| STD | 0.595 | 0.583 | 0.589 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 30( 62.5%) | 32( 61.5%) | 62( 62.0%) |
| >= 800,000 IU/mL | 18( 37.5%) | 20( 38.5%) | 38( 38.0%) |
| Baseline Genotype | | | |
| 1a | 28( 58.3%) | 30( 57.7%) | 58( 58.0%) |
| 1b | 17( 35.4%) | 19( 36.5%) | 36( 36.0%) |
| 4 | 1( 2.1%) | .( . %) | 1( 1.0%) |
| 4a/4c/4d | 1( 2.1%) | 2( 3.8%) | 3( 3.0%) |
| 4e | .( . %) | 1( 1.9%) | 1( 1.0%) |
| 4h | 1( 2.1%) | .( . %) | 1( 1.0%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 30.05 (0.972) | 28.16 (0.675) | 29.07 (0.589) |
| Median | 28.93 | 27.73 | 27.87 |
| Range | (19.49, 48.53) | (18.67, 42.48) | (18.67, 48.53) |
| STD | 6.735 | 4.866 | 5.885 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 29( 60.4%) | 37( 71.2%) | 66( 66.0%) |
| >= 30 kg/m2 | 19( 39.6%) | 15( 28.8%) | 34( 34.0%) |
| Baseline Cirrhosis Status | | | |
| Y | 48(100.0%) | 52(100.0%) | 100(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 59.67 (4.430) | 64.87 (4.012) | 62.37 (2.975) |
| Median | 52.00 | 56.00 | 54.50 |
| Range | (18.00, 184.0) | (21.00, 146.0) | (18.00, 184.0) |
| STD | 30.69 | 28.93 | 29.75 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 28( 58.3%) | 33( 63.5%) | 61( 61.0%) |
| > 1.5 x ULN | 20( 41.7%) | 19( 36.5%) | 39( 39.0%) |
| Baseline CPT Score | | | |
| Mean (SE) | 10.31 (0.152) | 10.44 (0.115) | 10.38 (0.094) |
| Median | 10.00 | 10.00 | 10.00 |
| Range | ( 8.00, 12.00) | ( 9.00, 12.00) | ( 8.00, 12.00) |
| STD | 1.055 | 0.826 | 0.940 |
| Baseline CPT Category | | | |
| CPT B | 12( 25.0%) | 5( 9.6%) | 17( 17.0%) |
| CPT C | 36( 75.0%) | 47( 90.4%) | 83( 83.0%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline MELD Score | | | |
| Mean (SE) | 14.94 (0.459) | 15.54 (0.408) | 15.25 (0.306) |
| Median | 15.00 | 15.00 | 15.00 |
| Range | ( 8.00, 23.00) | (10.00, 24.00) | ( 8.00, 24.00) |
| STD | 3.178 | 2.940 | 3.056 |
| Baseline MELD Category | | | |
| <10 | 2( 4.2%) | .( . %) | 2( 2.0%) |
| 10-15 | 27( 56.3%) | 28( 53.8%) | 55( 55.0%) |
| 16-20 | 17( 35.4%) | 21( 40.4%) | 38( 38.0%) |
| 21-25 | 2( 4.2%) | 3( 5.8%) | 5( 5.0%) |
| IL28B genotype | | | |
| CC | 13( 27.1%) | 11( 21.2%) | 24( 24.0%) |
| CT | 23( 47.9%) | 30( 57.7%) | 53( 53.0%) |
| TT | 12( 25.0%) | 11( 21.2%) | 23( 23.0%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 24( 50.0%) | 36( 69.2%) | 60( 60.0%) |
| Treatment-naive | 24( 50.0%) | 16( 30.8%) | 40( 40.0%) |
| Prior Response Category | | | |
| n | 23 | 36 | 59 |
| Non-Responder | 17( 73.9%) | 24( 66.7%) | 41( 69.5%) |
| Relapse/Breakthrough | 6( 26.1%) | 12( 33.3%) | 18( 30.5%) |
| Prior Treatment | | | |
| n | 24 | 36 | 60 |
| Other | 2( 8.3%) | 3( 8.3%) | 5( 8.3%) |
| PEG + RBV | 17( 70.8%) | 30( 83.3%) | 47( 78.3%) |
| PI + PEG + RBV | 5( 20.8%) | 3( 8.3%) | 8( 13.3%) |
| Baseline GFR | | | |
| Mean (SE) | 76.27 (3.168) | 90.82 (4.678) | 83.84 (2.947) |
| Median | 76.73 | 85.97 | 80.04 |
| Range | (36.08, 132.6) | (42.09, 223.6) | (36.08, 223.6) |
| STD | 21.95 | 33.73 | 29.47 |
| Country | | | |
| AUS | 7( 14.6%) | 4( 7.7%) | 11( 11.0%) |
| AUT | 1( 2.1%) | .( . %) | 1( 1.0%) |
| BEL | 3( 6.3%) | .( . %) | 3( 3.0%) |
| CAN | 4( 8.3%) | 1( 1.9%) | 5( 5.0%) |
| CHE | 1( 2.1%) | 2( 3.8%) | 3( 3.0%) |
| DEU | 3( 6.3%) | 3( 5.8%) | 6( 6.0%) |
| ESP | 2( 4.2%) | 7( 13.5%) | 9( 9.0%) |
| FRA | 1( 2.1%) | 4( 7.7%) | 5( 5.0%) |
| GBR | .( . %) | 1( 1.9%) | 1( 1.0%) |
| ITA | 2( 4.2%) | 1( 1.9%) | 3( 3.0%) |
| NZL | 1( 2.1%) | 3( 5.8%) | 4( 4.0%) |
| USA | 23( 47.9%) | 26( 50.0%) | 49( 49.0%) |
| Region | | | |
| Non-US | 25( 52.1%) | 26( 50.0%) | 51( 51.0%) |
| US | 23( 47.9%) | 26( 50.0%) | 49( 49.0%) |



Reference ID: 3884456

**Table 53:** Demographics and Baseline Characteristics of Group 3 in Studies SOLAR-1 and SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 107 | 105 | 212 |
| Gender | | | |
| F | 21( 19.6%) | 20( 19.0%) | 41( 19.3%) |
| M | 86( 80.4%) | 85( 81.0%) | 171( 80.7%) |
| Race | | | |
| WHITE | 100( 93.5%) | 96( 91.4%) | 196( 92.5%) |
| AMERICAN INDIAN OR ALASKA NATIVE | 1( 0.9%) | 1( 1.0%) | 2( 0.9%) |
| ASIAN | .( . %) | 1( 1.0%) | 1( 0.5%) |
| BLACK OR AFRICAN AMERICAN | 5( 4.7%) | 4( 3.8%) | 9( 4.2%) |
| OTHER | 1( 0.9%) | 3( 2.9%) | 4( 1.9%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 8( 7.5%) | 14( 13.3%) | 22( 10.4%) |
| NOT HISPANIC OR LATINO | 99( 92.5%) | 91( 86.7%) | 190( 89.6%) |
| Age (Year) | | | |
| Mean (SE) | 58.5 (0.70) | 58.4 (0.65) | 58.5 (0.47) |
| Median | 59 | 58 | 59 |
| Range | (32, 72) | (26, 73) | (26, 73) |
| STD | 7.197 | 6.607 | 6.895 |
| Age Category | | | |
| < 65 | 86( 80.4%) | 91( 86.7%) | 177( 83.5%) |
| >= 65 | 21( 19.6%) | 14( 13.3%) | 35( 16.5%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.42 (0.065) | 6.45 (0.072) | 6.43 (0.048) |
| Median | 6.55 | 6.62 | 6.59 |
| Range | ( 3.80, 7.68) | ( 2.40, 7.83) | ( 2.40, 7.83) |
| STD | 0.669 | 0.739 | 0.703 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 22( 20.6%) | 15( 14.3%) | 37( 17.5%) |
| >= 800,000 IU/mL | 85( 79.4%) | 90( 85.7%) | 175( 82.5%) |
| Baseline Genotype | | | |
| 1a | 67( 62.6%) | 69( 65.7%) | 136( 64.2%) |
| 1b | 32( 29.9%) | 31( 29.5%) | 63( 29.7%) |
| 4 | 5( 4.7%) | 2( 1.9%) | 7( 3.3%) |
| 4a/4c/4d | 2( 1.9%) | 3( 2.9%) | 5( 2.4%) |
| 4h | 1( 0.9%) | .( . %) | 1( 0.5%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 28.63 (0.522) | 27.06 (0.405) | 27.85 (0.335) |
| Median | 27.69 | 26.64 | 27.36 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Range | (19.38, 47.22) | (17.88, 37.85) | (17.88, 47.22) |
| STD | 5.396 | 4.147 | 4.871 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 69( 64.5%) | 84( 80.0%) | 153( 72.2%) |
| >= 30 kg/m2 | 38( 35.5%) | 21( 20.0%) | 59( 27.8%) |
| Baseline Cirrhosis Status | | | |
| N | 107(100.0%) | 105(100.0%) | 212(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 83.80 (6.001) | 95.57 (8.435) | 89.63 (5.164) |
| Median | 66.00 | 69.00 | 68.50 |
| Range | (16.00, 271.0) | (12.00, 570.0) | (12.00, 570.0) |
| STD | 62.07 | 86.44 | 75.19 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 50( 46.7%) | 48( 45.7%) | 98( 46.2%) |
| > 1.5 x ULN | 57( 53.3%) | 57( 54.3%) | 114( 53.8%) |
| Baseline CPT Score | | | |
| n | 107 | 104 | 211 |
| Mean (SE) | 5.36 (0.065) | 5.24 (0.048) | 5.30 (0.041) |
| Median | 5.00 | 5.00 | 5.00 |
| Range | ( 5.00, 9.00) | ( 5.00, 7.00) | ( 5.00, 9.00) |
| STD | 0.676 | 0.493 | 0.594 |
| Baseline CPT Category | | | |
| n | 107 | 104 | 211 |
| CPT A | 100( 93.5%) | 101( 97.1%) | 201( 95.3%) |
| CPT B | 7( 6.5%) | 3( 2.9%) | 10( 4.7%) |
| Baseline MELD Score | | | |
| n | 107 | 104 | 211 |
| Mean (SE) | 9.72 (0.313) | 8.79 (0.232) | 9.26 (0.198) |
| Median | 9.00 | 8.50 | 9.00 |
| Range | ( 6.00, 24.00) | ( 6.00, 17.00) | ( 6.00, 24.00) |
| STD | 3.235 | 2.363 | 2.871 |
| Baseline MELD Category | | | |
| <10 | 58( 54.2%) | 69( 65.7%) | 127( 59.9%) |
| 10-15 | 41( 38.3%) | 34( 32.4%) | 75( 35.4%) |
| 16-20 | 7( 6.5%) | 2( 1.9%) | 9( 4.2%) |
| 21-25 | 1( 0.9%) | .( . %) | 1( 0.5%) |
| IL28B genotype | | | |
| CC | 20( 18.7%) | 20( 19.0%) | 40( 18.9%) |
| CT | 64( 59.8%) | 52( 49.5%) | 116( 54.7%) |
| TT | 23( 21.5%) | 33( 31.4%) | 56( 26.4%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 80( 74.8%) | 84( 80.0%) | 164( 77.4%) |
| Treatment-naive | 27( 25.2%) | 21( 20.0%) | 48( 22.6%) |
| Prior Response Category | | | |
| n | 80 | 83 | 163 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Non-Responder | 51( 63.8%) | 49( 59.0%) | 100( 61.3%) |
| Relapse/Breakthrough | 29( 36.3%) | 34( 41.0%) | 63( 38.7%) |
| **Prior Treatment** | | | |
| n | 80 | 84 | 164 |
| PEG + RBV | 61( 76.3%) | 63( 75.0%) | 124( 75.6%) |
| PI + PEG + RBV | 14( 17.5%) | 15( 17.9%) | 29( 17.7%) |
| **Baseline GFR** | | | |
| Mean (SE) | 63.20 (1.632) | 68.01 (1.721) | 65.58 (1.194) |
| Median | 60.80 | 68.65 | 62.97 |
| Range | (20.44, 113.3) | (34.39, 116.8) | (20.44, 116.8) |
| STD | 16.88 | 17.63 | 17.38 |
| **Country** | | | |
| AUS | .( . %) | 2( 1.9%) | 2( 0.9%) |
| AUT | 8( 7.5%) | 2( 1.9%) | 10( 4.7%) |
| BEL | 3( 2.8%) | 3( 2.9%) | 6( 2.8%) |
| CAN | 8( 7.5%) | 6( 5.7%) | 14( 6.6%) |
| CHE | 4( 3.7%) | 3( 2.9%) | 7( 3.3%) |
| DEU | 6( 5.6%) | 5( 4.8%) | 11( 5.2%) |
| ESP | 4( 3.7%) | 8( 7.6%) | 12( 5.7%) |
| FRA | 4( 3.7%) | 5( 4.8%) | 9( 4.2%) |
| GBR | 8( 7.5%) | 9( 8.6%) | 17( 8.0%) |
| ITA | 2( 1.9%) | 2( 1.9%) | 4( 1.9%) |
| NLD | 3( 2.8%) | 4( 3.8%) | 7( 3.3%) |
| NZL | 2( 1.9%) | .( . %) | 2( 0.9%) |
| USA | 55( 51.4%) | 56( 53.3%) | 111( 52.4%) |
| **Region** | | | |
| Non-US | 52( 48.6%) | 49( 46.7%) | 101( 47.6%) |
| US | 55( 51.4%) | 56( 53.3%) | 111( 52.4% |

**Table 54:** Demographics and Baseline Characteristics of Group 4 in Studies SOLAR-1 and SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| **Treated (ITT)** | | | |
| N | 60 | 58 | 118 |
| **Gender** | | | |
| F | 13( 21.7%) | 10( 17.2%) | 23( 19.5%) |
| M | 47( 78.3%) | 48( 82.8%) | 95( 80.5%) |
| **Race** | | | |
| WHITE | 54( 90.0%) | 50( 86.2%) | 104( 88.1%) |
| BLACK OR AFRICAN AMERICAN | 3( 5.0%) | 4( 6.9%) | 7( 5.9%) |
| ASIAN | .( . %) | 4( 6.9%) | 4( 3.4%) |
| AMERICAN INDIAN OR ALASKA NATIVE | 1( 1.7%) | .( . %) | 1( 0.8%) |
| NATIVE HAWAIIAN OR PACIFIC ISLANDER | 1( 1.7%) | .( . %) | 1( 0.8%) |
| OTHER | 1( 1.7%) | .( . %) | 1( 0.8%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Ethnicity | | | |
| HISPANIC OR LATINO | 7( 11.7%) | 9( 15.5%) | 16( 13.6%) |
| NOT HISPANIC OR LATINO | 53( 88.3%) | 49( 84.5%) | 102( 86.4%) |
| Age (Year) | | | |
| Mean (SE) | 58.7 (0.90) | 61.4 (1.16) | 60.0 (0.74) |
| Median | 58 | 61.5 | 59.5 |
| Range | (33, 78) | (21, 81) | (21, 81) |
| STD | 6.954 | 8.799 | 7.996 |
| Age Category | | | |
| < 65 | 49( 81.7%) | 37( 63.8%) | 86( 72.9%) |
| >= 65 | 11( 18.3%) | 21( 36.2%) | 32( 27.1%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.28 (0.086) | 6.58 (0.064) | 6.43 (0.056) |
| Median | 6.37 | 6.62 | 6.48 |
| Range | ( 4.57, 7.55) | ( 4.68, 7.53) | ( 4.57, 7.55) |
| STD | 0.667 | 0.489 | 0.603 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 16( 26.7%) | 5( 8.6%) | 21( 17.8%) |
| >= 800,000 IU/mL | 44( 73.3%) | 53( 91.4%) | 97( 82.2%) |
| Baseline Genotype | | | |
| 1a | 31( 51.7%) | 30( 51.7%) | 61( 51.7%) |
| 1b | 25( 41.7%) | 23( 39.7%) | 48( 40.7%) |
| 4 | 3( 5.0%) | 2( 3.4%) | 5( 4.2%) |
| 4a/4c/4d | 1( 1.7%) | 3( 5.2%) | 4( 3.4%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 28.12 (0.673) | 26.91 (0.560) | 27.53 (0.441) |
| Median | 27.74 | 26.40 | 27.06 |
| Range | (18.72, 43.46) | (17.59, 36.95) | (17.59, 43.46) |
| STD | 5.210 | 4.264 | 4.787 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 38( 63.3%) | 45( 77.6%) | 83( 70.3%) |
| >= 30 kg/m2 | 22( 36.7%) | 13( 22.4%) | 35( 29.7%) |
| Baseline Cirrhosis Status | | | |
| Y | 60(100.0%) | 58(100.0%) | 118(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 91.05 (7.624) | 91.91 (9.455) | 91.47 (6.026) |
| Median | 68.00 | 75.00 | 72.50 |
| Range | (23.00, 264.0) | (17.00, 355.0) | (17.00, 355.0) |
| STD | 59.05 | 72.00 | 65.46 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 24( 40.0%) | 25( 43.1%) | 49( 41.5%) |
| > 1.5 x ULN | 36( 60.0%) | 33( 56.9%) | 69( 58.5%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline CPT Score | | | |
| Mean (SE) | 5.47 (0.073) | 5.53 (0.079) | 5.50 (0.053) |
| Median | 5.00 | 5.00 | 5.00 |
| Range | ( 5.00, 7.00) | ( 5.00, 7.00) | ( 5.00, 7.00) |
| STD | 0.566 | 0.599 | 0.581 |
| Baseline CPT Category | | | |
| CPT A | 58( 96.7%) | 55( 94.8%) | 113( 95.8%) |
| CPT B | 2( 3.3%) | 3( 5.2%) | 5( 4.2%) |
| Baseline MELD Score | | | |
| Mean (SE) | 9.42 (0.325) | 9.66 (0.349) | 9.53 (0.238) |
| Median | 9.00 | 9.00 | 9.00 |
| Range | ( 6.00, 16.00) | ( 6.00, 20.00) | ( 6.00, 20.00) |
| STD | 2.520 | 2.659 | 2.581 |
| Baseline MELD Category | | | |
| <10 | 34( 56.7%) | 30( 51.7%) | 64( 54.2%) |
| 10-15 | 25( 41.7%) | 26( 44.8%) | 51( 43.2%) |
| 16-20 | 1( 1.7%) | 2( 3.4%) | 3( 2.5%) |
| IL28B genotype | | | |
| CC | 10( 16.7%) | 8( 13.8%) | 18( 15.3%) |
| CT | 34( 56.7%) | 40( 69.0%) | 74( 62.7%) |
| TT | 16( 26.7%) | 10( 17.2%) | 26( 22.0%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 53( 88.3%) | 53( 91.4%) | 106( 89.8%) |
| Treatment-naive | 7( 11.7%) | 5( 8.6%) | 12( 10.2%) |
| Prior Response Category | | | |
| n | 53 | 53 | 106 |
| Non-Responder | 31( 58.5%) | 36( 67.9%) | 67( 63.2%) |
| Relapse/Breakthrough | 22( 41.5%) | 17( 32.1%) | 39( 36.8%) |
| Prior Treatment | | | |
| n | 53 | 53 | 106 |
| Other | 6( 11.3%) | 5( 9.4%) | 11( 10.4%) |
| PEG + RBV | 37( 69.8%) | 38( 71.7%) | 75( 70.8%) |
| PI + PEG + RBV | 10( 18.9%) | 10( 18.9%) | 20( 18.9%) |
| Baseline GFR | | | |
| Mean (SE) | 64.77 (2.418) | 67.09 (2.768) | 65.91 (1.829) |
| Median | 62.08 | 65.54 | 62.84 |
| Range | (29.24, 123.5) | (26.76, 132.1) | (26.76, 132.1) |
| STD | 18.73 | 21.08 | 19.87 |
| Country | | | |
| AUS | 3( 5.0%) | 3( 5.2%) | 6( 5.1%) |
| AUT | 2( 3.3%) | 3( 5.2%) | 5( 4.2%) |
| BEL | 1( 1.7%) | 1( 1.7%) | 2( 1.7%) |
| CAN | 4( 6.7%) | 5( 8.6%) | 9( 7.6%) |
| CHE | 4( 6.7%) | 2( 3.4%) | 6( 5.1%) |
| DEU | .( . %) | 3( 5.2%) | 3( 2.5%) |
| ESP | 5( 8.3%) | 5( 8.6%) | 10( 8.5%) |
| FRA | 6( 10.0%) | 3( 5.2%) | 9( 7.6%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| GBR | 4( 6.7%) | 5( 8.6%) | 9( 7.6%) |
| ITA | 3( 5.0%) | 1( 1.7%) | 4( 3.4%) |
| NZL | 2( 3.3%) | 2( 3.4%) | 4( 3.4%) |
| USA | 26( 43.3%) | 25( 43.1%) | 51( 43.2%) |
| Region | | | |
| Non-US | 34( 56.7%) | 33( 56.9%) | 67( 56.8%) |
| US | 26( 43.3%) | 25( 43.1%) | 51( 43.2%) |

**Table 55:** Demographics and Baseline Characteristics of Group 5 in Studies SOLAR-1 and SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 48 | 49 | 97 |
| Gender | | | |
| F | 11( 22.9%) | 11( 22.4%) | 22( 22.7%) |
| M | 37( 77.1%) | 38( 77.6%) | 75( 77.3%) |
| Race | | | |
| WHITE | 42( 87.5%) | 45( 91.8%) | 87( 89.7%) |
| BLACK OR AFRICAN AMERICAN | 5( 10.4%) | 3( 6.1%) | 8( 8.2%) |
| ASIAN | .( . %) | 1( 2.0%) | 1( 1.0%) |
| OTHER | 1( 2.1%) | .( . %) | 1( 1.0%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 8( 16.7%) | 7( 14.3%) | 15( 15.5%) |
| NOT HISPANIC OR LATINO | 40( 83.3%) | 42( 85.7%) | 82( 84.5%) |
| Age (Year) | | | |
| Mean (SE) | 58.3 (0.99) | 60.6 (1.20) | 59.5 (0.78) |
| Median | 59 | 61 | 60 |
| Range | (41, 76) | (23, 74) | (22, 76) |
| STD | 6.851 | 8.411 | 7.723 |
| Age Category | | | |
| < 65 | 42( 87.5%) | 36( 73.5%) | 78( 80.4%) |
| >= 65 | 6( 12.5%) | 13( 26.5%) | 19( 19.6%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.20 (0.096) | 6.22 (0.107) | 6.21 (0.072) |
| Median | 6.29 | 6.37 | 6.36 |
| Range | ( 3.71, 7.12) | ( 3.40, 7.38) | ( 3.40, 7.38) |
| STD | 0.663 | 0.752 | 0.706 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 11( 22.9%) | 18( 36.7%) | 29( 29.9%) |
| >= 800,000 IU/mL | 37( 77.1%) | 31( 63.3%) | 68( 70.1%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline Genotype | | | |
| 1a | 31( 64.6%) | 31( 63.3%) | 62( 63.9%) |
| 1b | 15( 31.3%) | 14( 28.6%) | 29( 29.9%) |
| 4 | .( . %) | 4( 8.2%) | 4( 4.1%) |
| 4a/4c/4d | 2( 4.2%) | .( . %) | 2( 2.1%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 27.17 (0.676) | 27.09 (0.566) | 27.13 (0.438) |
| Median | 25.72 | 26.81 | 26.51 |
| Range | (19.27, 39.56) | (18.98, 37.79) | (18.98, 39.56) |
| STD | 4.683 | 3.961 | 4.311 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 32( 66.7%) | 40( 81.6%) | 72( 74.2%) |
| >= 30 kg/m2 | 16( 33.3%) | 9( 18.4%) | 25( 25.8%) |
| Baseline Cirrhosis Status | | | |
| Y | 48(100.0%) | 49(100.0%) | 97(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 80.96 (7.843) | 83.71 (8.157) | 82.35 (5.633) |
| Median | 65.00 | 74.00 | 66.00 |
| Range | (14.00, 228.0) | (12.00, 254.0) | (12.00, 254.0) |
| STD | 54.34 | 57.10 | 55.47 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 22( 45.8%) | 21( 42.9%) | 43( 44.3%) |
| > 1.5 x ULN | 26( 54.2%) | 28( 57.1%) | 54( 55.7%) |
| Baseline CPT Score | | | |
| Mean (SE) | 7.71 (0.133) | 7.49 (0.149) | 7.60 (0.100) |
| Median | 8.00 | 7.00 | 8.00 |
| Range | ( 5.00, 10.00) | ( 5.00, 11.00) | ( 5.00, 11.00) |
| STD | 0.922 | 1.043 | 0.986 |
| Baseline CPT Category | | | |
| CPT A | 3( 6.3%) | 4( 8.2%) | 7( 7.2%) |
| CPT B | 43( 89.6%) | 43( 87.8%) | 86( 88.7%) |
| CPT C | 2( 4.2%) | 2( 4.1%) | 4( 4.1%) |
| Baseline MELD Score | | | |
| Mean (SE) | 11.79 (0.533) | 11.80 (0.479) | 11.79 (0.356) |
| Median | 11.00 | 12.00 | 11.00 |
| Range | ( 6.00, 23.00) | ( 6.00, 20.00) | ( 6.00, 23.00) |
| STD | 3.696 | 3.354 | 3.509 |
| Baseline MELD Category | | | |
| <10 | 13( 27.1%) | 12( 24.5%) | 25( 25.8%) |
| 10-15 | 27( 56.3%) | 32( 65.3%) | 59( 60.8%) |
| 16-20 | 6( 12.5%) | 5( 10.2%) | 11( 11.3%) |
| 21-25 | 2( 4.2%) | .( . %) | 2( 2.1%) |
| IL28B genotype | | | |
| CC | 6( 12.5%) | 10( 20.4%) | 16( 16.5%) |
| CT | 26( 54.2%) | 27( 55.1%) | 53( 54.6%) |
| TT | 16( 33.3%) | 12( 24.5%) | 28( 28.9%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Prior Treatment Category | | | |
| Treatment-experienced | 40( 83.3%) | 41( 83.7%) | 81( 83.5%) |
| Treatment-naive | 8( 16.7%) | 8( 16.3%) | 16( 16.5%) |
| Prior Response Category | | | |
| n | 40 | 41 | 81 |
| Non-Responder | 31( 77.5%) | 31( 75.6%) | 62( 76.5%) |
| Relapse/Breakthrough | 9( 22.5%) | 10( 24.4%) | 19( 23.5%) |
| Prior Treatment | | | |
| n | 40 | 41 | 81 |
| Other | 9( 22.5%) | 3( 7.3%) | 12( 14.8%) |
| PEG + RBV | 21( 52.5%) | 31( 75.6%) | 52( 64.2%) |
| PI + PEG + RBV | 10( 25.0%) | 7( 17.1%) | 17( 21.0%) |
| Baseline GFR | | | |
| Mean (SE) | 70.72 (3.282) | 61.95 (2.919) | 66.29 (2.227) |
| Median | 70.24 | 56.82 | 63.83 |
| Range | (30.36, 118.9) | (29.03, 123.9) | (29.03, 123.9) |
| STD | 22.74 | 20.43 | 21.94 |
| Country | | | |
| AUS | 2( 4.2%) | 2( 4.1%) | 4( 4.1%) |
| AUT | 1( 2.1%) | 2( 4.1%) | 3( 3.1%) |
| BEL | .( . %) | 2( 4.1%) | 2( 2.1%) |
| CAN | 4( 8.3%) | 5( 10.2%) | 9( 9.3%) |
| CHE | 2( 4.2%) | .( . %) | 2( 2.1%) |
| DEU | 1( 2.1%) | 1( 2.0%) | 2( 2.1%) |
| ESP | 3( 6.3%) | 4( 8.2%) | 7( 7.2%) |
| FRA | 3( 6.3%) | 3( 6.1%) | 6( 6.2%) |
| ITA | 3( 6.3%) | 3( 6.1%) | 6( 6.2%) |
| NLD | 1( 2.1%) | .( . %) | 1( 1.0%) |
| NZL | 2( 4.2%) | 1( 2.0%) | 3( 3.1%) |
| USA | 26( 54.2%) | 26( 53.1%) | 52( 53.6%) |
| Region | | | |
| Non-US | 22( 45.8%) | 23( 46.9%) | 45( 46.4%) |
| US | 26( 54.2%) | 26( 53.1%) | 52( 53.6%) |

**Table 56:** Demographics and Baseline Characteristics of Group 6 in Studies SOLAR-1 and SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 8 | 9 | 17 |
| Gender | | | |
| F | 1( 12.5%) | .( . %) | 1( 5.9%) |
| M | 7( 87.5%) | 9(100.0%) | 16( 94.1%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Race | | | |
| WHITE | 7( 87.5%) | 9(100.0%) | 16( 94.1%) |
| BLACK OR AFRICAN AMERICAN | 1( 12.5%) | .( . %) | 1( 5.9%) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 4( 50.0%) | 2( 22.2%) | 6( 35.3%) |
| NOT HISPANIC OR LATINO | 4( 50.0%) | 7( 77.8%) | 11( 64.7%) |
| Age (Year) | | | |
| Mean (SE) | 60.9 (1.37) | 61.2 (2.21) | 61.1 (1.30) |
| Median | 60 | 61 | 61 |
| Range | (57, 66) | (52, 75) | (52, 75) |
| STD | 3.871 | 6.629 | 5.344 |
| Age Category | | | |
| < 65 | 6( 75.0%) | 7( 77.8%) | 13( 76.5%) |
| >= 65 | 2( 25.0%) | 2( 22.2%) | 4( 23.5%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.24 (0.158) | 6.38 (0.144) | 6.31 (0.104) |
| Median | 6.26 | 6.37 | 6.34 |
| Range | ( 5.70, 6.81) | ( 5.91, 7.27) | ( 5.70, 7.27) |
| STD | 0.446 | 0.432 | 0.431 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 3( 37.5%) | .( . %) | 3( 17.6%) |
| >= 800,000 IU/mL | 5( 62.5%) | 9(100.0%) | 14( 82.4%) |
| Baseline Genotype | | | |
| 1a | 5( 62.5%) | 4( 44.4%) | 9( 52.9%) |
| 1b | 2( 25.0%) | 5( 55.6%) | 7( 41.2%) |
| 4 | 1( 12.5%) | .( . %) | 1( 5.9%) |
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 28.12 (2.064) | 25.84 (1.847) | 26.91 (1.364) |
| Median | 26.53 | 23.97 | 25.54 |
| Range | (20.08, 38.73) | (20.21, 35.11) | (20.08, 38.73) |
| STD | 5.838 | 5.542 | 5.624 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 5( 62.5%) | 7( 77.8%) | 12( 70.6%) |
| >= 30 kg/m2 | 3( 37.5%) | 2( 22.2%) | 5( 29.4%) |
| Baseline Cirrhosis Status | | | |
| Y | 8(100.0%) | 9(100.0%) | 17(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 59.50 (7.869) | 89.00 (20.81) | 75.12 (11.87) |
| Median | 63.00 | 55.00 | 55.00 |
| Range | (24.00, 85.00) | (21.00, 201.0) | (21.00, 201.0) |
| STD | 22.26 | 62.43 | 48.95 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline ALT Category | | | |
| <= 1.5 x ULN | 4( 50.0%) | 4( 44.4%) | 8( 47.1%) |
| > 1.5 x ULN | 4( 50.0%) | 5( 55.6%) | 9( 52.9%) |
| Baseline CPT Score | | | |
| Mean (SE) | 10.50 (0.423) | 9.89 (0.200) | 10.18 (0.231) |
| Median | 10.50 | 10.00 | 10.00 |
| Range | ( 9.00, 12.00) | ( 9.00, 11.00) | ( 9.00, 12.00) |
| STD | 1.195 | 0.601 | 0.951 |
| Baseline CPT Category | | | |
| CPT B | 2( 25.0%) | 2( 22.2%) | 4( 23.5%) |
| CPT C | 6( 75.0%) | 7( 77.8%) | 13( 76.5%) |
| Baseline MELD Score | | | |
| Mean (SE) | 14.25 (1.398) | 15.22 (0.862) | 14.76 (0.784) |
| Median | 14.00 | 15.00 | 15.00 |
| Range | ( 8.00, 19.00) | (13.00, 21.00) | ( 8.00, 21.00) |
| STD | 3.955 | 2.587 | 3.231 |
| Baseline MELD Category | | | |
| <10 | 1( 12.5%) | .( . %) | 1( 5.9%) |
| 10-15 | 4( 50.0%) | 6( 66.7%) | 10( 58.8%) |
| 16-20 | 3( 37.5%) | 2( 22.2%) | 5( 29.4%) |
| 21-25 | .( . %) | 1( 11.1%) | 1( 5.9%) |
| IL28B genotype | | | |
| CC | 2( 25.0%) | 4( 44.4%) | 6( 35.3%) |
| CT | 4( 50.0%) | 4( 44.4%) | 8( 47.1%) |
| TT | 2( 25.0%) | 1( 11.1%) | 3( 17.6%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 6( 75.0%) | 9(100.0%) | 15( 88.2%) |
| Treatment-naive | 2( 25.0%) | .( . %) | 2( 11.8%) |
| Prior Response Category | | | |
| n | 6 | 9 | 15 |
| Non-Responder | 4( 66.7%) | 5( 55.6%) | 9( 60.0%) |
| Relapse/Breakthrough | 2( 33.3%) | 4( 44.4%) | 6( 40.0%) |
| Prior Treatment | | | |
| n | 6 | 9 | 15 |
| Other | .( . %) | 2( 22.2%) | 2( 13.3%) |
| PEG + RBV | 6(100.0%) | 6( 66.7%) | 12( 80.0%) |
| PI + PEG + RBV | .( . %) | 1( 11.1%) | 1( 6.7%) |
| Baseline GFR | | | |
| Mean (SE) | 71.41 (6.360) | 59.69 (4.684) | 65.20 (4.034) |
| Median | 66.62 | 55.36 | 66.58 |
| Range | (54.00, 100.4) | (39.51, 81.07) | (39.51, 100.4) |
| STD | 17.99 | 14.05 | 16.63 |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Country | | | |
| AUS | .( . %) | 1( 11.1%) | 1( 5.9%) |
| ESP | 1( 12.5%) | 2( 22.2%) | 3( 17.6%) |
| GBR | 1( 12.5%) | .( . %) | 1( 5.9%) |
| ITA | 1( 12.5%) | 2( 22.2%) | 3( 17.6%) |
| USA | 5( 62.5%) | 4( 44.4%) | 9( 52.9%) |
| Region | | | |
| Non-US | 3( 37.5%) | 5( 55.6%) | 8( 47.1%) |
| US | 5( 62.5%) | 4( 44.4%) | 9( 52.9%) |

**Table 57:** Demographics and Baseline Characteristics of Group 7 in Studies SOLAR-1 and SOLAR-2 (Safety)

| Subgroup | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 7 | 4 | 11 |
| Gender | | | |
| F | 1( 14.3%) | 1( 25.0%) | 2( 18.2%) |
| M | 6( 85.7%) | 3( 75.0%) | 9( 81.8%) |
| Race | | | |
| WHITE | 6( 85.7%) | 3( 75.0%) | 9( 81.8%) |
| ASIAN | 1( 14.3%) | 1( 25.0%) | 2( 18.2%) |
| Ethnicity | | | |
| NOT HISPANIC OR LATINO | 7(100.0%) | 4(100.0%) | 11(100.0%) |
| Age (Year) | | | |
| Mean (SE) | 60.1 (1.28) | 57.0 (2.65) | 59.0 (1.27) |
| Median | 59 | 56 | 59 |
| Range | (56, 65) | (52, 64) | (52, 65) |
| STD | 3.388 | 5.292 | 4.219 |
| Age Category | | | |
| < 65 | 6( 85.7%) | 4(100.0%) | 10( 90.9%) |
| >= 65 | 1( 14.3%) | .( . %) | 1( 9.1%) |
| Baseline HCV RNA log10 (IU/mL) | | | |
| Mean (SE) | 6.85 (0.401) | 6.55 (0.409) | 6.74 (0.286) |
| Median | 6.56 | 6.37 | 6.56 |
| Range | ( 4.94, 7.99) | ( 5.75, 7.69) | ( 4.94, 7.99) |
| STD | 1.061 | 0.817 | 0.948 |
| Baseline HCV RNA Category 1 (IU/mL) | | | |
| < 800,000 IU/mL | 1( 14.3%) | 1( 25.0%) | 2( 18.2%) |
| >= 800,000 IU/mL | 6( 85.7%) | 3( 75.0%) | 9( 81.8%) |
| Baseline Genotype | | | |
| 1a | 5( 71.4%) | 4(100.0%) | 9( 81.8%) |
| 1b | 2( 28.6%) | .( . %) | 2( 18.2%) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Baseline BMI (kg/m^2) | | | |
| Mean (SE) | 23.43 (1.515) | 23.84 (0.552) | 23.58 (0.956) |
| Median | 24.47 | 23.90 | 23.91 |
| Range | (17.56, 30.24) | (22.42, 25.12) | (17.56, 30.24) |
| STD | 4.009 | 1.103 | 3.170 |
| Baseline BMI Category (kg/m2) | | | |
| < 30 kg/m2 | 6( 85.7%) | 4(100.0%) | 10( 90.9%) |
| >= 30 kg/m2 | 1( 14.3%) | .( . %) | 1( 9.1%) |
| Baseline Cirrhosis Status | | | |
| N | 7(100.0%) | 4(100.0%) | 11(100.0%) |
| Baseline ALT | | | |
| Mean (SE) | 161.1 (18.21) | 152.8 (34.82) | 158.1 (16.14) |
| Median | 174.0 | 164.5 | 174.0 |
| Range | (71.00, 211.0) | (62.00, 220.0) | (62.00, 220.0) |
| STD | 48.19 | 69.63 | 53.53 |
| Baseline ALT Category | | | |
| <= 1.5 x ULN | .( . %) | 1( 25.0%) | 1( 9.1%) |
| > 1.5 x ULN | 7(100.0%) | 3( 75.0%) | 10( 90.9%) |
| Baseline CPT Score | | | |
| Mean (SE) | 8.29 (0.360) | 8.25 (0.854) | 8.27 (0.359) |
| Median | 8.00 | 8.50 | 8.00 |
| Range | ( 7.00, 10.00) | ( 6.00, 10.00) | ( 6.00, 10.00) |
| STD | 0.951 | 1.708 | 1.191 |
| Baseline CPT Category | | | |
| CPT A | .( . %) | 1( 25.0%) | 1( 9.1%) |
| CPT B | 6( 85.7%) | 2( 50.0%) | 8( 72.7%) |
| CPT C | 1( 14.3%) | 1( 25.0%) | 2( 18.2%) |
| Baseline MELD Score | | | |
| n | 6 | 3 | 9 |
| Mean (SE) | 15.00 (1.571) | 15.00 (3.464) | 15.00 (1.424) |
| Median | 15.00 | 15.00 | 15.00 |
| Range | ( 9.00, 19.00) | ( 9.00, 21.00) | ( 9.00, 21.00) |
| STD | 3.847 | 6.000 | 4.272 |
| Baseline MELD Category | | | |
| <10 | 2( 28.6%) | 2( 50.0%) | 4( 36.4%) |
| 10-15 | 2( 28.6%) | 1( 25.0%) | 3( 27.3%) |
| 16-20 | 3( 42.9%) | .( . %) | 3( 27.3%) |
| 21-25 | .( . %) | 1( 25.0%) | 1( 9.1%) |
| IL28B genotype | | | |
| CC | .( . %) | 1( 25.0%) | 1( 9.1%) |
| CT | 5( 71.4%) | 2( 50.0%) | 7( 63.6%) |
| TT | 2( 28.6%) | 1( 25.0%) | 3( 27.3%) |
| Prior Treatment Category | | | |
| Treatment-experienced | 6( 85.7%) | 3( 75.0%) | 9( 81.8%) |
| Treatment-naive | 1( 14.3%) | 1( 25.0%) | 2( 18.2%) |



Reference ID: 3884456

```
Prior Response Category
  n                                 6                 3                 9
  Non-Responder             6(100.0%)         2( 66.7%)         8( 88.9%)
  Relapse/Breakthrough      .(    . %)        1( 33.3%)         1( 11.1%)

Prior Treatment
  n                                 6                 3                 9
  PEG + RBV                 6(100.0%)         3(100.0%)         9(100.0%)

Baseline GFR
  n                                 6                 3                 9
  Mean (SE)              80.06 (9.015)     82.20 (10.42)     80.77 (6.560)
  Median                        88.92             75.26             88.09
  Range                (36.00,  93.89)   (68.64,  102.7)   (36.00,  102.7)
  STD                           22.08             18.05             19.68
Country
  AUS                       .(    . %)        1( 25.0%)         1(  9.1%)
  CAN                       .(    . %)        1( 25.0%)         1(  9.1%)
  FRA                       1( 14.3%)         .(    . %)        1(  9.1%)
  NZL                       2( 28.6%)         .(    . %)        2( 18.2%)
  USA                       4( 57.1%)         2( 50.0%)         6( 54.5%)

Region
  Non-US                    3( 42.9%)         2( 50.0%)         5( 45.5%)
  US                        4( 57.1%)         2( 50.0%)         6( 54.5%)
-----------------------------------------------------------------------------
```

**Table 58:** Primary Efficacy Results (SVR12) by Group for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Cohort | Group | T12WK | T24WK |
|---|---|---|---|
| **A (pre-transplant)** | **G1: CPT B** | **85.7% (48/56)** | **92.3% (48/52)** |
| | G2: CPT C | 83.7% (36/43) | 81.3% (39/48) |
| B (Post-transplant) | G3: F0-F3 Fibrosis | 95.3% (102/107) | 99.1% (104/105) |
| | G4: CPT A | 96.7% (58/60) | 96.6% (56/58) |
| | **G5: CPT B** | 89.6% (43/48) | 93.9% (46/49) |
| | G6: CPT C | 50.0% (4/8) | 77.8% (7/9) |
| | G7: FCH | 100% (7/7) | 100% (4/4) |

**Table 59:** SVR12 Rate by Group Combination (Pre vs. Post) for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Transplant Status | Cirrhosis Status | 12 Weeks | 24 Weeks |
|---|---|---|---|
| Pre-transplanted (CPT B / C) | Decompensated (G1+G2) | 84.9% (84/89) | 87.0% (87/100) |
| Post-transplanted (CPT B / C) | Decompensated (G5+G6) | 83.9% (47/56) | 91.4% (53/58) |
| Post-transplanted (CPT A) | Compensated (G3+G4) | 95.8% (160/167) | 98.2% (160/163) |

**Table 60:** SVR12 Rate by Group Combination (CPT Category) for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| CPT Category | Cirrhosis Status | 12 Weeks | 24 Weeks |
|---|---|---|---|
| CPT B | Decompensated (G1+G5) | 87.5% (91/104) | 93.1% (94/101) |
| CPT C | Decompensated (G2+G6) | 78.4% (40/51) | 80.7% (46/57) |
| **CPT B/C** | **Decompensated (G1+G5+G2+G6)** | **84.5% (131/155)** | **88.6% (140/158)** |



Reference ID: 3884456

**Table 61:** The MELD Score Changes at FU-12 Weeks from Baseline for Subjects who Received 12 Weeks Treatment and Had SVR12=Success in Groups 1, 2, 5, and 6 of SOLAR-1 and SOLAR-2 Combined.

| FU week 12 outcome | MELD | MELD | MELD | MELD | MELD | |
|---|---|---|---|---|---|---|
| | <10 | 10-15 | 16-20 | 21-25 | >25 | |
| Achieved SVR12 (N=123) (5 missed CPT information) | | | | | | |
| Improvement in MELD from baseline | 6 | 46 | 17 | 1 | | 56.9% |
| N=123 No change in MELD from baseline | 4 | 17 | 2 | 0 | | 18.7% |
| Worse MELD from baseline | 11 | 15 | 3 | 1 | | 24.4% |
| | | | | | | |
| Improvement in CPT class at FU week 12 | 9 | 24 | 6 | 1 | | 33.9% |
| N=118 No change in CPT class at FU week 12 | 12 | 51 | 13 | | | 64.4% |
| Worse in CPT class at FU week 12 | | 2 | | | | 1.7% |

**Table 62:** The MELD Score Changes at FU-12 Weeks from Baseline for Subjects who Received 12 Weeks Treatment and Had SVR12=Failure in Groups 1, 2, 5, and 6 of SOLAR-1 and SOLAR-2 Combined.

| FU week 12 outcome | MELD | MELD | MELD | MELD | MELD |
|---|---|---|---|---|---|
| | <10 | 10-15 | 16-20 | 21-25 | >25 |
| Not achieve SVR12 (N=4) (one missed CPT information) | | | | | |
| Improvement in MELD from baseline | | 3 | | | |
| No change in MELD from baseline | | | | | |
| Worse MELD from baseline | | 1 | | | |
| | | | | | |
| Improvement in CPT class at FU week 12 | | 2 | | | |
| No change in CPT class at FU week 12 | | 1 | | | |
| worse in CPT class at FU week 12 | | | | | |

**4 subjects out of these 127 subjects has failed as relapsers at SVR12. (GT1=3)**



Reference ID: 3884456

**Table 63:** The CPT Category Changes at FU-12 Weeks from Baseline for Subjects who Received 12 Weeks Treatment in Groups 1, 2, 5, and 6 of SOLAR-1 and SOLAR-2 Combined.

| Meld at Baseline | Category Change for CPT from Baseline to FU12 | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | C to A | C to B | B to A | A to A | B to B | C to C | A to B | B to C |
| <10 | 1 | 1 | 7 | 1 | 11 | | | |
| 10-15 | | 9 | 15 | 2 | 45 | 4 | | 2 |
| 16-20 | | 6 | | | 8 | 5 | | |
| 21-25 | | 1 | | | | | | |

For these 123 subjects who met SVR12, 118 subjects listed in the table, 5 subjects missed CPT information. 3 subjects had CPT=A at baseline.

**Table 64:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 1 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Efficacy Parameter | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 45/ 52(86.5) | 46/ 50(92.0) | 91/102(89.2) |
| Gender | | | |
| F | 12 / 12 ( 100) | 17 / 19 (89.5) | 29 / 31 (93.5) |
| M | 33 / 40 (82.5) | 29 / 31 (93.5) | 62 / 71 (87.3) |
| Race | | | |
| WHITE | 44 / 49 (89.8) | 43 / 47 (91.5) | 87 / 96 (90.6) |
| BLACK OR AFRICA AMERICAN | . / 1 (0.00) | 3 / 3 ( 100) | 3 / 4 (75.0) |
| NATIVE HAWAIIAN OR ALASKA NATIVE | . / 1 (0.00) | . / . ( . ) | . / . ( . ) |
| OTHER | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 8 / 10 (80.0) | 8 / 9 (88.9) | 16 / 19 (84.2) |
| NOT HISPANIC OR LATINO | 37 / 42 (88.1) | 38 / 41 (92.7) | 75 / 83 (90.4) |
| Age Group 1 | | | |
| < 65 | 41 / 48 (85.4) | 41 / 45 (91.1) | 82 / 93 (88.2) |
| >= 65 | 4 / 4 ( 100) | 5 / 5 ( 100) | 9 / 9 ( 100) |
| HCV RNA BSL <800K | | | |
| < 800,000 IU/mL | 20 / 22 (90.9) | 20 / 22 (90.9) | 40 / 44 (90.9) |
| >= 800,000 IU/mL | 25 / 30 (83.3) | 26 / 28 (92.9) | 51 / 58 (87.9) |
| MELD Category at Baseline | | | |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| <10 | 7 / 7 ( 100) | 13 / 13 ( 100) | 20 / 20 ( 100) |
| 10-15 | 33 / 39 (84.6) | 28 / 31 (90.3) | 61 / 70 (87.1) |
| 16-20 | 5 / 6 (83.3) | 5 / 6 (83.3) | 10 / 12 (83.3) |
| HCV Genotype | | | |
| 1a | 28 / 31 (90.3) | 30 / 32 (93.8) | 58 / 63 (92.1) |
| 1b | 17 / 21 (81.0) | 16 / 18 (88.9) | 33 / 39 (84.6) |
| BMI category | | | |
| < 30 kg/m2 | 34 / 38 (89.5) | 34 / 37 (91.9) | 68 / 75 (90.7) |
| >= 30 kg/m2 | 11 / 14 (78.6) | 12 / 13 (92.3) | 23 / 27 (85.2) |
| CPT Category at Baseline | | | |
| CPT A | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| CPT B | 43 / 49 (87.8) | 43 / 47 (91.5) | 86 / 96 (89.6) |
| CPT C | 2 / 3 (66.7) | 2 / 2 ( 100) | 4 / 5 (80.0) |
| IL28B Genotype | | | |
| CC | 8 / 9 (88.9) | 12 / 12 ( 100) | 20 / 21 (95.2) |
| CT | 29 / 34 (85.3) | 25 / 25 ( 100) | 54 / 59 (91.5) |
| TT | 8 / 9 (88.9) | 9 / 13 (69.2) | 17 / 22 (77.3) |
| Prior Treatment Category | | | |
| Treatment-experienced | 35 / 41 (85.4) | 34 / 37 (91.9) | 69 / 78 (88.5) |
| Treatment-naive | 10 / 11 (90.9) | 12 / 13 (92.3) | 22 / 24 (91.7) |
| Prior Response Category | | | |
| Non-Responder | 24 / 30 (80.0) | 21 / 24 (87.5) | 45 / 54 (83.3) |
| Relapse/Breakthrough | 10 / 10 ( 100) | 12 / 12 ( 100) | 22 / 22 ( 100) |
| Prior Treatment | | | |
| Other | 5 / 5 ( 100) | 1 / 1 ( 100) | 6 / 6 ( 100) |
| PEG + RBV | 20 / 24 (83.3) | 22 / 25 (88.0) | 42 / 49 (85.7) |
| PI + PEG + RBV | 10 / 12 (83.3) | 11 / 11 ( 100) | 21 / 23 (91.3) |
| Country | | | |
| AUS | 1 / 1 ( 100) | 1 / 1 ( 100) | 2 / 2 ( 100) |
| AUT | 1 / 1 ( 100) | 1 / 1 ( 100) | 2 / 2 ( 100) |
| BEL | 1 / 1 ( 100) | 2 / 2 ( 100) | 3 / 3 ( 100) |
| CAN | 6 / 6 ( 100) | 5 / 5 ( 100) | 11 / 11 ( 100) |
| CHE | . / 1 (0.00) | 2 / 2 ( 100) | 2 / 3 (66.7) |
| DEU | 1 / 1 ( 100) | 3 / 3 ( 100) | 4 / 4 ( 100) |
| ESP | 5 / 6 (83.3) | 4 / 5 (80.0) | 9 / 11 (81.8) |
| FRA | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| GBR | 3 / 3 ( 100) | 2 / 2 ( 100) | 5 / 5 ( 100) |
| ITA | 2 / 2 ( 100) | 1 / 1 ( 100) | 3 / 3 ( 100) |
| NZL | . / 1 (0.00) | . / . ( . ) | . / . ( . ) |
| USA | 25 / 29 (86.2) | 24 / 27 (88.9) | 49 / 56 (87.5) |



Reference ID: 3884456

**Table 65:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 2 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Efficacy Parameter | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 35/ 40(87.5) | 38/ 46(82.6) | 73/ 86(84.9) |
| Gender | | | |
| F | 16 / 18 (88.9) | 11 / 13 (84.6) | 27 / 31 (87.1) |
| M | 19 / 22 (86.4) | 27 / 33 (81.8) | 46 / 55 (83.6) |
| Race | | | |
| WHITE | 33 / 37 (89.2) | 37 / 43 (86.0) | 70 / 80 (87.5) |
| BLACK OR AFRICA AMERICAN | 2 / 2 ( 100) | . / 2 (0.00) | 2 / 4 (50.0) |
| OTHER | . / 1 (0.00) | 1 / 1 ( 100) | 1 / 2 (50.0) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 4 / 5 (80.0) | 9 / 11 (81.8) | 13 / 16 (81.3) |
| NOT HISPANIC OR LATINO | 31 / 35 (88.6) | 29 / 35 (82.9) | 60 / 70 (85.7) |
| Age Group 1 | | | |
| < 65 | 31 / 36 (86.1) | 32 / 39 (82.1) | 63 / 75 (84.0) |
| >= 65 | 4 / 4 ( 100) | 6 / 7 (85.7) | 10 / 11 (90.9) |
| HCV RNA BSL <800K | | | |
| < 800,000 IU/mL | 21 / 24 (87.5) | 22 / 28 (78.6) | 43 / 52 (82.7) |
| >= 800,000 IU/mL | 14 / 16 (87.5) | 16 / 18 (88.9) | 30 / 34 (88.2) |
| MELD Category at Baseline | | | |
| <10 | 2 / 2 ( 100) | . / . ( . ) | 2 / 2 ( 100) |
| 10-15 | 20 / 23 (87.0) | 23 / 26 (88.5) | 43 / 49 (87.8) |
| 16-20 | 12 / 14 (85.7) | 12 / 17 (70.6) | 24 / 31 (77.4) |
| 21-25 | 1 / 1 ( 100) | 3 / 3 ( 100) | 4 / 4 ( 100) |
| MELD Category at Baseline - 1 | | | |
| <10 | 2 / 2 ( 100) | . / . ( . ) | 2 / 2 ( 100) |
| >=10- <15 | 14 / 16 (87.5) | 19 / 21 (90.5) | 33 / 37 (89.2) |
| >=15 | 19 / 22 (86.4) | 19 / 25 (76.0) | 38 / 47 (80.9) |
| HCV Genotype | | | |
| 1a | 21 / 24 (87.5) | 21 / 27 (77.8) | 42 / 51 (82.4) |
| 1b | 14 / 16 (87.5) | 17 / 19 (89.5) | 31 / 35 (88.6) |
| BMI category | | | |
| < 30 kg/m2 | 21 / 23 (91.3) | 27 / 31 (87.1) | 48 / 54 (88.9) |
| >= 30 kg/m2 | 14 / 17 (82.4) | 11 / 15 (73.3) | 25 / 32 (78.1) |
| CPT Category at Baseline | | | |
| CPT B | 8 / 9 (88.9) | 3 / 4 (75.0) | 11 / 13 (84.6) |
| CPT C | 27 / 31 (87.1) | 35 / 42 (83.3) | 62 / 73 (84.9) |
| IL28B Genotype | | | |
| CC | 9 / 11 (81.8) | 8 / 10 (80.0) | 17 / 21 (81.0) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| CT | 16 / 19 (84.2) | 23 / 28 (82.1) | 39 / 47 (83.0) |
| TT | 10 / 10 ( 100) | 7 / 8 (87.5) | 17 / 18 (94.4) |
| Prior Treatment Category | | | |
| Treatment-experienced | 19 / 22 (86.4) | 24 / 31 (77.4) | 43 / 53 (81.1) |
| Treatment-naive | 16 / 18 (88.9) | 14 / 15 (93.3) | 30 / 33 (90.9) |
| Prior Response Category | | | |
| Non-Responder | 12 / 15 (80.0) | 18 / 22 (81.8) | 30 / 37 (81.1) |
| Relapse/Breakthrough | 6 / 6 ( 100) | 6 / 9 (66.7) | 12 / 15 (80.0) |
| Prior Treatment | | | |
| Other | 1 / 2 (50.0) | 2 / 3 (66.7) | 3 / 5 (60.0) |
| PEG + RBV | 15 / 16 (93.8) | 21 / 25 (84.0) | 36 / 41 (87.8) |
| PI + PEG + RBV | 3 / 4 (75.0) | 1 / 3 (33.3) | 4 / 7 (57.1) |
| Country | | | |
| AUS | 6 / 7 (85.7) | 4 / 4 ( 100) | 10 / 11 (90.9) |
| AUT | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| BEL | 2 / 2 ( 100) | . / . ( . ) | 2 / 2 ( 100) |
| CAN | 2 / 2 ( 100) | 1 / 1 ( 100) | 3 / 3 ( 100) |
| CHE | 1 / 1 ( 100) | 2 / 2 ( 100) | 3 / 3 ( 100) |
| DEU | 2 / 3 (66.7) | 3 / 3 ( 100) | 5 / 6 (83.3) |
| ESP | 2 / 2 ( 100) | 5 / 7 (71.4) | 7 / 9 (77.8) |
| FRA | 1 / 1 ( 100) | . / 1 (0.00) | 1 / 2 (50.0) |
| GBR | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| ITA | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| NZL | . / 1 (0.00) | 1 / 3 (33.3) | 1 / 4 (25.0) |
| USA | 18 / 20 (90.0) | 20 / 23 (87.0) | 38 / 43 (88.4) |

**Table 66:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 3 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Efficacy Parameter | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 94/ 99(94.9) | 99/100(99.0) | 193/199(97.0) |
| Gender | | | |
| F | 18 / 19 (94.7) | 19 / 19 ( 100) | 37 / 38 (97.4) |
| M | 76 / 80 (95.0) | 80 / 81 (98.8) | 156 /161 (96.9) |
| Race | | | |
| WHITE | 88 / 93 (94.6) | 91 / 91 ( 100) | 179 /184 (97.3) |
| BLACK OR AFRICA AMERICAN | 4 / 4 ( 100) | 3 / 4 (75.0) | 7 / 8 (87.5) |
| OTHER | 1 / 1 ( 100) | 3 / 3 ( 100) | 4 / 4 ( 100) |
| AMERICAN INDIAN OR ALASKA NATIVE | 1 / 1 ( 100) | 1 / 1 ( 100) | 2 / 2 ( 100) |
| ASIAN | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| Ethnicity | | | |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| HISPANIC OR LATINO | 7 / 8 (87.5) | 13 / 13 ( 100) | 20 / 21 (95.2) |
| NOT HISPANIC OR LATINO | 87 / 91 (95.6) | 86 / 87 (98.9) | 173 /178 (97.2) |
| Age Group 1 | | | |
| < 65 | 77 / 80 (96.3) | 85 / 86 (98.8) | 162 /166 (97.6) |
| >= 65 | 17 / 19 (89.5) | 14 / 14 ( 100) | 31 / 33 (93.9) |
| HCV RNA BSL <800K | | | |
| < 800,000 IU/mL | 21 / 21 ( 100) | 14 / 14 ( 100) | 35 / 35 ( 100) |
| >= 800,000 IU/mL | 73 / 78 (93.6) | 85 / 86 (98.8) | 158 /164 (96.3) |
| MELD Category at Baseline | | | |
| <10 | 49 / 52 (94.2) | 66 / 66 ( 100) | 115 /118 (97.5) |
| 10-15 | 38 / 39 (97.4) | 31 / 32 (96.9) | 69 / 71 (97.2) |
| 16-20 | 6 / 7 (85.7) | 2 / 2 ( 100) | 8 / 9 (88.9) |
| 21-25 | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| MELD Category at Baseline - 1 | | | |
| <10 | 49 / 52 (94.2) | 66 / 66 ( 100) | 115 /118 (97.5) |
| >=10- <15 | 38 / 39 (97.4) | 30 / 31 (96.8) | 68 / 70 (97.1) |
| >=15 | 7 / 8 (87.5) | 3 / 3 ( 100) | 10 / 11 (90.9) |
| HCV Genotype | | | |
| 1a | 63 / 67 (94.0) | 68 / 69 (98.6) | 131 /136 (96.3) |
| 1b | 31 / 32 (96.9) | 31 / 31 ( 100) | 62 / 63 (98.4) |
| BMI category | | | |
| < 30 kg/m2 | 57 / 61 (93.4) | 79 / 79 ( 100) | 136 /140 (97.1) |
| >= 30 kg/m2 | 37 / 38 (97.4) | 20 / 21 (95.2) | 57 / 59 (96.6) |
| CPT Category at Baseline | | | |
| CPT A | 88 / 92 (95.7) | 95 / 96 (99.0) | 183 /188 (97.3) |
| CPT B | 6 / 7 (85.7) | 3 / 3 ( 100) | 9 / 10 (90.0) |
| IL28B Genotype | | | |
| CC | 17 / 18 (94.4) | 20 / 20 ( 100) | 37 / 38 (97.4) |
| CT | 56 / 60 (93.3) | 47 / 47 ( 100) | 103 /107 (96.3) |
| TT | 21 / 21 ( 100) | 32 / 33 (97.0) | 53 / 54 (98.1) |
| Prior Treatment Category | | | |
| Treatment-experienced | 70 / 73 (95.9) | 79 / 80 (98.8) | 149 /153 (97.4) |
| Treatment-naive | 24 / 26 (92.3) | 20 / 20 ( 100) | 44 / 46 (95.7) |
| Prior Response Category | | | |
| Non-Responder | 43 / 45 (95.6) | 47 / 48 (97.9) | 90 / 93 (96.8) |
| Relapse/Breakthrough | 27 / 28 (96.4) | 31 / 31 ( 100) | 58 / 59 (98.3) |
| Prior Treatment | | | |
| Other | 5 / 5 ( 100) | 6 / 6 ( 100) | 11 / 11 ( 100) |
| PEG + RBV | 51 / 54 (94.4) | 58 / 59 (98.3) | 109 /113 (96.5) |
| PI + PEG + RBV | 14 / 14 ( 100) | 15 / 15 ( 100) | 29 / 29 ( 100) |
| Country | | | |
| AUS | . / . ( . ) | 2 / 2 ( 100) | 2 / 2 ( 100) |
| AUT | 6 / 6 ( 100) | 2 / 2 ( 100) | 8 / 8 ( 100) |
| BEL | 2 / 2 ( 100) | 3 / 3 ( 100) | 5 / 5 ( 100) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| CAN | 8 / 8 ( 100) | 6 / 6 ( 100) | 14 / 14 ( 100) |
| CHE | 2 / 3 (66.7) | 3 / 3 ( 100) | 5 / 6 (83.3) |
| DEU | 6 / 6 ( 100) | 5 / 5 ( 100) | 11 / 11 ( 100) |
| ESP | 3 / 4 (75.0) | 7 / 7 ( 100) | 10 / 11 (90.9) |
| FRA | 3 / 4 (75.0) | 4 / 4 ( 100) | 7 / 8 (87.5) |
| GBR | 7 / 7 ( 100) | 8 / 8 ( 100) | 15 / 15 ( 100) |
| ITA | 1 / 1 ( 100) | 2 / 2 ( 100) | 3 / 3 ( 100) |
| NLD | 2 / 2 ( 100) | 2 / 2 ( 100) | 4 / 4 ( 100) |
| NZL | 2 / 2 ( 100) | . / . ( . ) | 2 / 2 ( 100) |
| USA | 52 / 54 (96.3) | 55 / 56 (98.2) | 107 /110 (97.3) |

**Table 67:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 4 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Efficacy Parameter | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 55/ 56(98.2) | 51/ 53(96.2) | 106/109(97.2) |
| Gender | | | |
| F | 13 / 13 ( 100) | 10 / 10 ( 100) | 23 / 23 ( 100) |
| M | 42 / 43 (97.7) | 41 / 43 (95.3) | 83 / 86 (96.5) |
| Race | | | |
| WHITE | 49 / 50 (98.0) | 44 / 45 (97.8) | 93 / 95 (97.9) |
| BLACK OR AFRICA AMERICAN | 3 / 3 ( 100) | 4 / 4 ( 100) | 7 / 7 ( 100) |
| ASIAN | . / . ( . ) | 3 / 4 (75.0) | 3 / 4 (75.0) |
| AMERICAN INDIAN OR ALASKA NATIVE | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| NATIVE HAWAIIAN OR PACIFIC ISLANDER | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| OTHER | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 6 / 6 ( 100) | 7 / 7 ( 100) | 13 / 13 ( 100) |
| NOT HISPANIC OR LATINO | 49 / 50 (98.0) | 44 / 46 (95.7) | 93 / 96 (96.9) |
| Age Group 1 | | | |
| < 65 | 47 / 47 ( 100) | 32 / 33 (97.0) | 79 / 80 (98.8) |
| >= 65 | 8 / 9 (88.9) | 19 / 20 (95.0) | 27 / 29 (93.1) |
| HCV RNA BSL <800K | | | |
| < 800,000 IU/mL | 13 / 14 (92.9) | 5 / 5 ( 100) | 18 / 19 (94.7) |
| >= 800,000 IU/mL | 42 / 42 ( 100) | 46 / 48 (95.8) | 88 / 90 (97.8) |
| MELD Category at Baseline | | | |
| <10 | 32 / 33 (97.0) | 29 / 30 (96.7) | 61 / 63 (96.8) |
| 10-15 | 22 / 22 ( 100) | 20 / 21 (95.2) | 42 / 43 (97.7) |
| 16-20 | 1 / 1 ( 100) | 2 / 2 ( 100) | 3 / 3 ( 100) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| HCV Genotype | | | |
| 1a | 30 / 31 (96.8) | 29 / 30 (96.7) | 59 / 61 (96.7) |
| 1b | 25 / 25 ( 100) | 22 / 23 (95.7) | 47 / 48 (97.9) |
| BMI category | | | |
| < 30 kg/m2 | 34 / 35 (97.1) | 38 / 40 (95.0) | 72 / 75 (96.0) |
| >= 30 kg/m2 | 21 / 21 ( 100) | 13 / 13 ( 100) | 34 / 34 ( 100) |
| CPT Category at Baseline | | | |
| CPT A | 53 / 54 (98.1) | 48 / 50 (96.0) | 101 /104 (97.1) |
| CPT B | 2 / 2 ( 100) | 3 / 3 ( 100) | 5 / 5 ( 100) |
| IL28B Genotype | | | |
| CC | 7 / 8 (87.5) | 8 / 8 ( 100) | 15 / 16 (93.8) |
| CT | 32 / 32 ( 100) | 33 / 35 (94.3) | 65 / 67 (97.0) |
| TT | 16 / 16 ( 100) | 10 / 10 ( 100) | 26 / 26 ( 100) |
| Prior Treatment Category | | | |
| Treatment-experienced | 49 / 50 (98.0) | 46 / 48 (95.8) | 95 / 98 (96.9) |
| Treatment-naive | 6 / 6 ( 100) | 5 / 5 ( 100) | 11 / 11 ( 100) |
| Prior Response Category | | | |
| Non-Responder | 29 / 30 (96.7) | 32 / 33 (97.0) | 61 / 63 (96.8) |
| Relapse/Breakthrough | 20 / 20 ( 100) | 14 / 15 (93.3) | 34 / 35 (97.1) |
| Prior Treatment | | | |
| Other | 6 / 6 ( 100) | 5 / 5 ( 100) | 11 / 11 ( 100) |
| PEG + RBV | 33 / 34 (97.1) | 31 / 33 (93.9) | 64 / 67 (95.5) |
| PI + PEG + RBV | 10 / 10 ( 100) | 10 / 10 ( 100) | 20 / 20 ( 100) |
| Country | | | |
| AUS | 2 / 2 ( 100) | 3 / 3 ( 100) | 5 / 5 ( 100) |
| AUT | 2 / 2 ( 100) | 2 / 2 ( 100) | 4 / 4 ( 100) |
| BEL | 1 / 1 ( 100) | 1 / 1 ( 100) | 2 / 2 ( 100) |
| CAN | 4 / 4 ( 100) | 4 / 4 ( 100) | 8 / 8 ( 100) |
| CHE | 2 / 2 ( 100) | 2 / 2 ( 100) | 4 / 4 ( 100) |
| DEU | . / . ( . ) | 3 / 3 ( 100) | 3 / 3 ( 100) |
| ESP | 4 / 4 ( 100) | 4 / 4 ( 100) | 8 / 8 ( 100) |
| FRA | 6 / 6 ( 100) | 3 / 3 ( 100) | 9 / 9 ( 100) |
| GBR | 4 / 4 ( 100) | 3 / 4 (75.0) | 7 / 8 (87.5) |
| ITA | 3 / 3 ( 100) | . / . ( . ) | 3 / 3 ( 100) |
| NZL | 2 / 2 ( 100) | 2 / 2 ( 100) | 4 / 4 ( 100) |
| USA | 25 / 26 (96.2) | 24 / 25 (96.0) | 49 / 51 (96.1) |

**Table 68:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 5 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Efficacy Parameter | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 41/ 46(89.1) | 43/ 45(95.6) | 84/ 91(92.3) |
| Gender | | | |
| F | 9 / 10 (90.0) | 10 / 10 ( 100) | 19 / 20 (95.0) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| M | 32 / 36 (88.9) | 33 / 35 (94.3) | 65 / 71 (91.5) |
| Race | | | |
| WHITE | 35 / 40 (87.5) | 40 / 42 (95.2) | 75 / 82 (91.5) |
| BLACK OR AFRICA AMERICAN | 5 / 5 ( 100) | 2 / 2 ( 100) | 7 / 7 ( 100) |
| ASIAN | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| OTHER | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 7 / 8 (87.5) | 7 / 7 ( 100) | 14 / 15 (93.3) |
| NOT HISPANIC OR LATINO | 34 / 38 (89.5) | 36 / 38 (94.7) | 70 / 76 (92.1) |
| Age Group 1 | | | |
| < 65 | 36 / 40 (90.0) | 31 / 32 (96.9) | 67 / 72 (93.1) |
| >= 65 | 5 / 6 (83.3) | 12 / 13 (92.3) | 17 / 19 (89.5) |
| HCV RNA BSL <800K | | | |
| < 800,000 IU/mL | 10 / 11 (90.9) | 13 / 14 (92.9) | 23 / 25 (92.0) |
| >= 800,000 IU/mL | 31 / 35 (88.6) | 30 / 31 (96.8) | 61 / 66 (92.4) |
| MELD Category at Baseline | | | |
| <10 | 12 / 12 ( 100) | 11 / 11 ( 100) | 23 / 23 ( 100) |
| 10-15 | 23 / 26 (88.5) | 28 / 30 (93.3) | 51 / 56 (91.1) |
| 16-20 | 5 / 6 (83.3) | 4 / 4 ( 100) | 9 / 10 (90.0) |
| 21-25 | 1 / 2 (50.0) | . / . ( . ) | 1 / 2 (50.0) |
| MELD Category at Baseline - 1 | | | |
| <10 | 12 / 12 ( 100) | 11 / 11 ( 100) | 23 / 23 ( 100) |
| >=10- <15 | 22 / 24 (91.7) | 25 / 27 (92.6) | 47 / 51 (92.2) |
| >=15 | 7 / 10 (70.0) | 7 / 7 ( 100) | 14 / 17 (82.4) |
| HCV Genotype | | | |
| 1a | 29 / 31 (93.5) | 30 / 31 (96.8) | 59 / 62 (95.2) |
| 1b | 12 / 15 (80.0) | 13 / 14 (92.9) | 25 / 29 (86.2) |
| BMI category | | | |
| < 30 kg/m2 | 27 / 30 (90.0) | 35 / 36 (97.2) | 62 / 66 (93.9) |
| >= 30 kg/m2 | 14 / 16 (87.5) | 8 / 9 (88.9) | 22 / 25 (88.0) |
| CPT Category at Baseline | | | |
| CPT A | 3 / 3 ( 100) | 3 / 3 ( 100) | 6 / 6 ( 100) |
| CPT B | 37 / 41 (90.2) | 39 / 41 (95.1) | 76 / 82 (92.7) |
| CPT C | 1 / 2 (50.0) | 1 / 1 ( 100) | 2 / 3 (66.7) |
| IL28B Genotype | | | |
| CC | 6 / 6 ( 100) | 9 / 9 ( 100) | 15 / 15 ( 100) |
| CT | 20 / 25 (80.0) | 26 / 27 (96.3) | 46 / 52 (88.5) |
| TT | 15 / 15 ( 100) | 8 / 9 (88.9) | 23 / 24 (95.8) |
| Prior Treatment Category | | | |
| Treatment-experienced | 35 / 38 (92.1) | 36 / 37 (97.3) | 71 / 75 (94.7) |
| Treatment-naive | 6 / 8 (75.0) | 7 / 8 (87.5) | 13 / 16 (81.3) |
| Prior Response Category | | | |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| Non-Responder | 27 / 29 (93.1) | 27 / 28 (96.4) | 54 / 57 (94.7) |
| Relapse/Breakthrough | 8 / 9 (88.9) | 9 / 9 ( 100) | 17 / 18 (94.4) |
| Prior Treatment | | | |
| Other | 9 / 9 ( 100) | 3 / 3 ( 100) | 12 / 12 ( 100) |
| PEG + RBV | 16 / 19 (84.2) | 26 / 27 (96.3) | 42 / 46 (91.3) |
| PI + PEG + RBV | 10 / 10 ( 100) | 7 / 7 ( 100) | 17 / 17 ( 100) |
| Country | | | |
| AUS | 2 / 2 ( 100) | 2 / 2 ( 100) | 4 / 4 ( 100) |
| AUT | 1 / 1 ( 100) | 2 / 2 ( 100) | 3 / 3 ( 100) |
| BEL | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| CAN | 4 / 4 ( 100) | 5 / 5 ( 100) | 9 / 9 ( 100) |
| CHE | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| DEU | 1 / 1 ( 100) | 1 / 1 ( 100) | 2 / 2 ( 100) |
| ESP | 2 / 3 (66.7) | 4 / 4 ( 100) | 6 / 7 (85.7) |
| FRA | 3 / 3 ( 100) | 2 / 2 ( 100) | 5 / 5 ( 100) |
| ITA | 2 / 2 ( 100) | 2 / 2 ( 100) | 4 / 4 ( 100) |
| NLD | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| NZL | 2 / 2 ( 100) | 1 / 1 ( 100) | 3 / 3 ( 100) |
| USA | 22 / 26 (84.6) | 23 / 25 (92.0) | 45 / 51 (88.2) |

**Table 69:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 6 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Efficacy Parameter | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 4/ 7(57.1) | 7/ 9(77.8) | 11/ 16(68.8) |
| Gender | | | |
| F | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| M | 3 / 6 (50.0) | 7 / 9 (77.8) | 10 / 15 (66.7) |
| Race | | | |
| WHITE | 3 / 6 (50.0) | 7 / 9 (77.8) | 10 / 15 (66.7) |
| BLACK OR AFRICA AMERICAN | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 2 / 4 (50.0) | 1 / 2 (50.0) | 3 / 6 (50.0) |
| NOT HISPANIC OR LATINO | 2 / 3 (66.7) | 6 / 7 (85.7) | 8 / 10 (80.0) |
| Age Group 1 | | | |
| < 65 | 2 / 5 (40.0) | 5 / 7 (71.4) | 7 / 12 (58.3) |
| >= 65 | 2 / 2 ( 100) | 2 / 2 ( 100) | 4 / 4 ( 100) |
| HCV RNA BSL <800K | | | |
| < 800,000 IU/mL | . / 2 (0.00) | . / . ( . ) | . / . ( . ) |
| >= 800,000 IU/mL | 4 / 5 (80.0) | 7 / 9 (77.8) | 11 / 14 (78.6) |
| MELD Category at Baseline | | | |
| <10 | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| 10-15 | 2 / 4 (50.0) | 5 / 6 (83.3) | 7 / 10 (70.0) |
| 16-20 | 1 / 2 (50.0) | 1 / 2 (50.0) | 2 / 4 (50.0) |
| 21-25 | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| MELD Category at Baseline - 1 | | | |
| <10 | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| >=10- <15 | 2 / 3 (66.7) | 4 / 4 ( 100) | 6 / 7 (85.7) |
| >=15 | 1 / 3 (33.3) | 3 / 5 (60.0) | 4 / 8 (50.0) |
| HCV Genotype | | | |
| 1a | 2 / 5 (40.0) | 2 / 4 (50.0) | 4 / 9 (44.4) |
| 1b | 2 / 2 ( 100) | 5 / 5 ( 100) | 7 / 7 ( 100) |
| BMI category | | | |
| < 30 kg/m2 | 3 / 4 (75.0) | 5 / 7 (71.4) | 8 / 11 (72.7) |
| >= 30 kg/m2 | 1 / 3 (33.3) | 2 / 2 ( 100) | 3 / 5 (60.0) |
| CPT Category at Baseline | | | |
| CPT B | 2 / 2 ( 100) | 2 / 2 ( 100) | 4 / 4 ( 100) |
| CPT C | 2 / 5 (40.0) | 5 / 7 (71.4) | 7 / 12 (58.3) |
| IL28B Genotype | | | |
| CC | 1 / 2 (50.0) | 3 / 4 (75.0) | 4 / 6 (66.7) |
| CT | 2 / 4 (50.0) | 3 / 4 (75.0) | 5 / 8 (62.5) |
| TT | 1 / 1 ( 100) | 1 / 1 ( 100) | 2 / 2 ( 100) |
| Prior Treatment Category | | | |
| Treatment-experienced | 3 / 6 (50.0) | 7 / 9 (77.8) | 10 / 15 (66.7) |
| Treatment-naive | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| Prior Response Category | | | |
| Non-Responder | 3 / 4 (75.0) | 4 / 5 (80.0) | 7 / 9 (77.8) |
| Relapse/Breakthrough | . / 2 (0.00) | 3 / 4 (75.0) | 3 / 6 (50.0) |
| Prior Treatment | | | |
| Other | . / . ( . ) | 1 / 2 (50.0) | 1 / 2 (50.0) |
| PEG + RBV | 3 / 6 (50.0) | 5 / 6 (83.3) | 8 / 12 (66.7) |
| PI + PEG + RBV | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| Country | | | |
| AUS | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| ESP | 1 / 1 ( 100) | 1 / 2 (50.0) | 2 / 3 (66.7) |
| GBR | . / 1 (0.00) | . / . ( . ) | . / . ( . ) |
| ITA | . / . ( . ) | 2 / 2 ( 100) | 2 / 2 ( 100) |
| USA | 3 / 5 (60.0) | 3 / 4 (75.0) | 6 / 9 (66.7) |



Reference ID: 3884456

**Table 70:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In Group 7 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Efficacy Parameter | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 7/ 7( 100) | 4/ 7( 100) | 11/ 11( 100) |
| Gender | | | |
| F | 1 / 1 ( 100) | 1 / 1 ( 100) | 2 / 2 ( 100) |
| M | 6 / 6 ( 100) | 3 / 3 ( 100) | 9 / 9 ( 100) |
| Race | | | |
| WHITE | 6 / 6 ( 100) | 3 / 3 ( 100) | 9 / 9 ( 100) |
| ASIAN | 1 / 1 ( 100) | 1 / 1 ( 100) | 2 / 2 ( 100) |
| Ethnicity | | | |
| NOT HISPANIC OR LATINO | 7 / 7 ( 100) | 4 / 4 ( 100) | 11 / 11 ( 100) |
| Age Group 1 | | | |
| < 65 | 6 / 6 ( 100) | 4 / 4 ( 100) | 10 / 10 ( 100) |
| >= 65 | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| HCV RNA BSL <800K | | | |
| < 800,000 IU/mL | 1 / 1 ( 100) | 1 / 1 ( 100) | 2 / 2 ( 100) |
| >= 800,000 IU/mL | 6 / 6 ( 100) | 3 / 3 ( 100) | 9 / 9 ( 100) |
| MELD Category at Baseline | | | |
| <10 | 2 / 2 ( 100) | 2 / 2 ( 100) | 4 / 4 ( 100) |
| 10-15 | 2 / 2 ( 100) | 1 / 1 ( 100) | 3 / 3 ( 100) |
| 16-20 | 3 / 3 ( 100) | . / . ( . ) | 3 / 3 ( 100) |
| 21-25 | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| MELD Category at Baseline - 1 | | | |
| <10 | 2 / 2 ( 100) | 2 / 2 ( 100) | 4 / 4 ( 100) |
| >=10- <15 | 2 / 2 ( 100) | . / . ( . ) | 2 / 2 ( 100) |
| >=15 | 3 / 3 ( 100) | 2 / 2 ( 100) | 5 / 5 ( 100) |
| HCV Genotype | | | |
| 1a | 5 / 5 ( 100) | 4 / 4 ( 100) | 9 / 9 ( 100) |
| 1b | 2 / 2 ( 100) | . / . ( . ) | 2 / 2 ( 100) |
| BMI category | | | |
| < 30 kg/m2 | 6 / 6 ( 100) | 4 / 4 ( 100) | 10 / 10 ( 100) |
| >= 30 kg/m2 | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| CPT Category at Baseline | | | |
| CPT A | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| CPT B | 6 / 6 ( 100) | 2 / 2 ( 100) | 8 / 8 ( 100) |
| CPT C | 1 / 1 ( 100) | 1 / 1 ( 100) | 2 / 2 ( 100) |
| IL28B Genotype | | | |
| CC | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| CT | 5 / 5 ( 100) | 2 / 2 ( 100) | 7 / 7 ( 100) |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| TT | 2 / 2 ( 100) | 1 / 1 ( 100) | 3 / 3 ( 100) |
| Prior Treatment Category | | | |
| Treatment-experienced | 6 / 6 ( 100) | 3 / 3 ( 100) | 9 / 9 ( 100) |
| Treatment-naive | 1 / 1 ( 100) | 1 / 1 ( 100) | 2 / 2 ( 100) |
| Prior Response Category | | | |
| Non-Responder | 6 / 6 ( 100) | 2 / 2 ( 100) | 8 / 8 ( 100) |
| Relapse/Breakthrough | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| Prior Treatment | | | |
| PEG + RBV | 6 / 6 ( 100) | 3 / 3 ( 100) | 9 / 9 ( 100) |
| Country | | | |
| AUS | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| CAN | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| FRA | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| NZL | 2 / 2 ( 100) | . / . ( . ) | 2 / 2 ( 100) |
| USA | 4 / 4 ( 100) | 2 / 2 ( 100) | 6 / 6 ( 100) |

**Table 71:** Subgroup Analyses of SVR12 of GT-1 Subjects Only In the combination of Group 1, 2, 5 and 6 of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Efficacy Parameter | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 125/145(86.2) | 134/150(89.3) | 259/295(87.8) |
| Gender | | | |
| F | 38 / 41 (92.7) | 38 / 42 (90.5) | 76 / 83 (91.6) |
| M | 87 /104 (83.7) | 96 /108 (88.9) | 183 /212 (86.3) |
| Race | | | |
| WHITE | 115 /132 (87.1) | 127 /141 (90.1) | 242 /273 (88.6) |
| BLACK OR AFRICA AMERICAN | 8 / 9 (88.9) | 5 / 7 (71.4) | 13 / 16 (81.3) |
| OTHER | 2 / 3 (66.7) | 1 / 1 ( 100) | 3 / 4 (75.0) |
| ASIAN | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| NATIVE HAWAIIAN OR PACIFIC ISLANDER | . / 1 (0.00) | . / . ( . ) | . / . ( . ) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 21 / 27 (77.8) | 25 / 29 (86.2) | 46 / 56 (82.1) |
| NOT HISPANIC OR LATINO | 104 /118 (88.1) | 109 /121 (90.1) | 213 /239 (89.1) |
| Age Group 1 | | | |
| < 65 | 110 /129 (85.3) | 109 /123 (88.6) | 219 /252 (86.9) |
| >= 65 | 15 / 16 (93.8) | 25 / 27 (92.6) | 40 / 43 (93.0) |
| HCV RNA BSL <800K | | | |
| < 800,000 IU/mL | 51 / 59 (86.4) | 55 / 64 (85.9) | 106 /123 (86.2) |
| >= 800,000 IU/mL | 74 / 86 (86.0) | 79 / 86 (91.9) | 153 /172 (89.0) |
| MELD Category at Baseline | | | |



Reference ID: 3884456

| | | | |
|---|---|---|---|
| <10 | 22 / 22 ( 100) | 24 / 24 ( 100) | 46 / 46 ( 100) |
| 10-15 | 78 / 92 (84.8) | 84 / 93 (90.3) | 162 /185 (87.6) |
| 16-20 | 23 / 28 (82.1) | 22 / 29 (75.9) | 45 / 57 (78.9) |
| 21-25 | 2 / 3 (66.7) | 4 / 4 ( 100) | 6 / 7 (85.7) |
| MELD Category at Baseline - 1 | | | |
| <10 | 22 / 22 ( 100) | 24 / 24 ( 100) | 46 / 46 ( 100) |
| >=10- <15 | 70 / 80 (87.5) | 75 / 82 (91.5) | 145 /162 (89.5) |
| >=15 | 33 / 43 (76.7) | 35 / 44 (79.5) | 68 / 87 (78.2) |
| HCV Genotype | | | |
| 1a | 80 / 91 (87.9) | 83 / 94 (88.3) | 163 /185 (88.1) |
| 1b | 45 / 54 (83.3) | 51 / 56 (91.1) | 96 /110 (87.3) |
| BMI category | | | |
| < 30 kg/m2 | 85 / 95 (89.5) | 101 /111 (91.0) | 186 /206 (90.3) |
| >= 30 kg/m2 | 40 / 50 (80.0) | 33 / 39 (84.6) | 73 / 89 (82.0) |
| CPT Category at Baseline | | | |
| CPT A | 3 / 3 ( 100) | 4 / 4 ( 100) | 7 / 7 ( 100) |
| CPT B | 90 /101 (89.1) | 87 / 94 (92.6) | 177 /195 (90.8) |
| CPT C | 32 / 41 (78.0) | 43 / 52 (82.7) | 75 / 93 (80.6) |
| IL28B Genotype | | | |
| CC | 24 / 28 (85.7) | 32 / 35 (91.4) | 56 / 63 (88.9) |
| CT | 67 / 82 (81.7) | 77 / 84 (91.7) | 144 /166 (86.7) |
| TT | 34 / 35 (97.1) | 25 / 31 (80.6) | 59 / 66 (89.4) |
| Prior Treatment Category | | | |
| Treatment-experienced | 92 /107 (86.0) | 101 /114 (88.6) | 193 /221 (87.3) |
| Treatment-naive | 33 / 38 (86.8) | 33 / 36 (91.7) | 66 / 74 (89.2) |
| Prior Response Category | | | |
| Non-Responder | 66 / 78 (84.6) | 70 / 79 (88.6) | 136 /157 (86.6) |
| Relapse/Breakthrough | 24 / 27 (88.9) | 30 / 34 (88.2) | 54 / 61 (88.5) |
| Prior Treatment | | | |
| Other | 15 / 16 (93.8) | 7 / 9 (77.8) | 22 / 25 (88.0) |
| PEG + RBV | 54 / 65 (83.1) | 74 / 83 (89.2) | 128 /148 (86.5) |
| PI + PEG + RBV | 23 / 26 (88.5) | 20 / 22 (90.9) | 43 / 48 (89.6) |
| Country | | | |
| AUS | 9 / 10 (90.0) | 8 / 8 ( 100) | 17 / 18 (94.4) |
| AUT | 3 / 3 ( 100) | 3 / 3 ( 100) | 6 / 6 ( 100) |
| BEL | 3 / 3 ( 100) | 3 / 3 ( 100) | 6 / 6 ( 100) |
| CAN | 12 / 12 ( 100) | 11 / 11 ( 100) | 23 / 23 ( 100) |
| CHE | 2 / 3 (66.7) | 4 / 4 ( 100) | 6 / 7 (85.7) |
| DEU | 4 / 5 (80.0) | 7 / 7 ( 100) | 11 / 12 (91.7) |
| ESP | 10 / 12 (83.3) | 14 / 18 (77.8) | 24 / 30 (80.0) |
| FRA | 4 / 4 ( 100) | 3 / 4 (75.0) | 7 / 8 (87.5) |
| GBR | 3 / 4 (75.0) | 3 / 3 ( 100) | 6 / 7 (85.7) |
| ITA | 4 / 4 ( 100) | 6 / 6 ( 100) | 10 / 10 ( 100) |
| NLD | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| NZL | 2 / 4 (50.0) | 2 / 4 (50.0) | 4 / 8 (50.0) |
| USA | 68 / 80 (85.0) | 70 / 79 (88.6) | 138 /159 (86.8) |



Reference ID: 3884456

**Table 72:** Primary Efficacy Results (SVR12) of GT-4 by Group for SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Cohort | Group | T12WK | T24WK |
|---|---|---|---|
| **A (pre-transplant)** | **G1: CPT B** | 75% (3/4) (19.4%, 99.4%) | 100% (2/2) (15.8%, 100.0%) |
| | G2: CPT C | 33% (1/3) (0.8%, 90.6%) | 50% (1/2) (1.3%, 98.7%) |
| B (Post-transplant) | G3: F0-F3 Fibrosis | 100% (8/8) (63.1%, 100.0%) | 100% (5/5) (47.8%, 100.0%) |
| | G4: CPT A | 75% (3/4) (19.4%, 99.4%) | 100% (5/5) (47.8%, 100.0%) |
| | **G5: CPT B** | 100% (2/2) (15.8%, 100.0%) | 75% (3/4) (19.4%, 99.4%) |
| | G6: CPT C | 0 (0/1) (0.0%, 97.5%) | 0 |
| | G7: FCH | 0 | 0 |

**Table 73:** Subgroup Analyses of SVR12 of GT-4 Subjects Only of Studies SOLAR-1 and SOLAR-2 (Efficacy Analysis Set)

| Efficacy Parameter | T12WK | T24WK | Total |
|---|---|---|---|
| Treated (ITT) | | | |
| N | 17/ 22(77.3) | 16/ 18(88.9) | 33/ 40(82.5) |
| Gender | | | |
| F | 4 / 5 (80.0) | 2 / 2 ( 100) | 6 / 7 (85.7) |
| M | 13 / 17 (76.5) | 14 / 16 (87.5) | 27 / 33 (81.8) |
| Race | | | |
| WHITE | 15 / 19 (78.9) | 15 / 17 (88.2) | 30 / 36 (83.3) |
| BLACK OR AFRICA AMERICAN | 2 / 3 (66.7) | 1 / 1 ( 100) | 3 / 4 (75.0) |
| Ethnicity | | | |
| HISPANIC OR LATINO | 1 / 1 ( 100) | 3 / 4 (75.0) | 4 / 5 (80.0) |
| NOT HISPANIC OR LATINO | 16 / 21 (76.2) | 13 / 14 (92.9) | 29 / 35 (82.9) |
| Age Group (years) | | | |
| < 65 | 11 / 16 (68.8) | 15 / 17 (88.2) | 26 / 33 (78.8) |
| >= 65 | 6 / 6 ( 100) | 1 / 1 ( 100) | 7 / 7 ( 100) |
| HCV RNA BSL <800K | | | |
| < 800,000 IU/mL | 4 / 8 (50.0) | 6 / 7 (85.7) | 10 / 15 (66.7) |
| >= 800,000 IU/mL | 13 / 14 (92.9) | 10 / 11 (90.9) | 23 / 25 (92.0) |
| MELD Category at Baseline | | | |
| <10 | 8 / 8 ( 100) | 3 / 4 (75.0) | 11 / 12 (91.7) |
| 10-15 | 8 / 11 (72.7) | 11 / 12 (91.7) | 19 / 23 (82.6) |
| 16-20 | 1 / 3 (33.3) | 2 / 2 ( 100) | 3 / 5 (60.0) |
| HCV Genotype | | | |
| 4 | 7 / 10 (70.0) | 9 / 10 (90.0) | 16 / 20 (80.0) |
| 4a | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| 4a/4c/4d | 7 / 8 (87.5) | 6 / 7 (85.7) | 13 / 15 (86.7) |
| 4e | . / . ( . ) | 1 / 1 ( 100) | 1 / 1 ( 100) |
| 4h | 1 / 2 (50.0) | . / . ( . ) | 1 / 2 (50.0) |
| 4r | 1 / 1 ( 100) | . / . ( . ) | 1 / 1 ( 100) |
| BMI category | | | |



Reference ID: 3884456

```
  <  30 kg/m2              16 / 20 (80.0)   15 / 17 (88.2)   31 / 37 (83.8)
  >= 30 kg/m2               1 /  2 (50.0)    1 /  1 ( 100)    2 /  3 (66.7)

CPT Category at Baseline
  CPT A                    11 / 12 (91.7)   10 / 11 (90.9)   21 / 23 (91.3)
  CPT B                     5 /  7 (71.4)    5 /  5 ( 100)   10 / 12 (83.3)
  CPT C                     1 /  3 (33.3)    1 /  2 (50.0)    2 /  5 (40.0)

IL28B Genotype
  CC                        4 /  6 (66.7)    1 /  3 (33.3)    5 /  9 (55.6)
  CT                        9 / 10 (90.0)   12 / 12 ( 100)   21 / 22 (95.5)
  TT                        4 /  6 (66.7)    3 /  3 ( 100)    7 /  9 (77.8)

Prior Treatment Category
  Treatment-experienced    14 / 17 (82.4)   14 / 16 (87.5)   28 / 33 (84.8)
  Treatment-naive           3 /  5 (60.0)    2 /  2 ( 100)    5 /  7 (71.4)

Prior Response Category
  Non-Responder            11 / 13 (84.6)    8 /  8 ( 100)   19 / 21 (90.5)
  Relapse/Breakthrough      3 /  4 (75.0)    6 /  8 (75.0)    9 / 12 (75.0)

Prior Treatment
  PEG + RBV                13 / 16 (81.3)   14 / 16 (87.5)   27 / 32 (84.4)
  PI + PEG + RBV            1 /  1 ( 100)    . /  . ( .  )    1 /  1 ( 100)

Country
  AUS                       . /  1 (0.00)    . /  . ( .  )    . /  . ( .  )
  AUT                       2 /  2 ( 100)    1 /  1 ( 100)    3 /  3 ( 100)
  BEL                       1 /  2 (50.0)    1 /  1 ( 100)    2 /  3 (66.7)
  CAN                       . /  . ( .  )    1 /  1 ( 100)    1 /  1 ( 100)
  CHE                       4 /  4 ( 100)    1 /  1 ( 100)    5 /  5 ( 100)
  DEU                       . /  1 (0.00)    1 /  1 ( 100)    1 /  2 (50.0)
  ESP                       1 /  1 ( 100)    2 /  2 ( 100)    3 /  3 ( 100)
  FRA                       1 /  1 ( 100)    3 /  4 (75.0)    4 /  5 (80.0)
  GBR                       2 /  2 ( 100)    2 /  2 ( 100)    4 /  4 ( 100)
  ITA                       2 /  3 (66.7)    2 /  2 ( 100)    4 /  5 (80.0)
  NLD                       1 /  1 ( 100)    2 /  2 ( 100)    3 /  3 ( 100)
  USA                       3 /  4 (75.0)    . /  1 (0.00)    3 /  5 (60.0)
-----------------------------------------------------------------------------
```

**Table 74:** SVR12 Rate of GT-1 by Group Combination (Pre vs. Post) for SOLAR-1 and SOLAR-2 without 12 Principal Investigators Data (Efficacy Analysis Set)

| Transplant Status | Cirrhosis Status | T12WK | T24WK |
|---|---|---|---|
| Pre-transplanted (CPT B / C) | Decompensated (G1+G2) | 90.4% (66/73) | 84.0% (63/75) |
| Post-transplanted (CPT B / C) | Decompensated (G5+G6) | 81.8% (36/44) | 97.4% (38/39) |
| Post-transplanted (CPT A) | Compensated (G3+G4) | 95.1% (117/123) | 99.2% (120/121) |

**Table 75:** SVR12 Rate of GT-1 by Group Combination (CPT Category) for SOLAR-1 and SOLAR-2 without 12 Principal Investigators Data (Efficacy Analysis Set)

| CPT Category | Cirrhosis Status | T12WK | T24WK |
|---|---|---|---|
| CPT B | Decompensated (G1+G5) | 87.5% (70/80) | 94.5% (69/73) |
| CPT C | Decompensated (G2+G6) | 86.5% (32/37) | 78.1% (32/41) |
| **CPT B/C** | **Decompensated (G1+G5+G2+G6)** | **87.2% (102/117)** | **88.6% (101/114)** |



Reference ID: 3884456

## References

1. StatXact PROCs User Manual for SAS Users, Version 6, 2004, Cytel.
2. SAS Version 9.3, SAS Inc.
3. Sofosbuvir label;



Reference ID: 3884456

---

**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

---

/s/

---

WEN ZENG
02/08/2016

THAMBAN I VALAPPIL
02/09/2016