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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: 206,843 / S-0001, S-0002, and S-0003

Drug Name: Daclatasvir (DCV) tablet: 30 mg or 60 mg

Indication(s): The treatment of Chronic Hepatitis C Infection in Adults

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1. EXECUTIVE SUMMARY

Daclatasvir (BMS-790052; abbreviated as DCV) was originally approved on July 24, 2015 for use with sofosbuvir for the treatment of chronic HCV genotype 3 infection. The recommended dose is 60 mg once daily (QD) administered with Sofosbuvir (SOF, or called Sovaldi™). This efficacy supplement proposes to extend the indication to support the use of DCV plus SOF with or without ribavirin for the treatment of chronic HCV infected, including those coinfecting with human immunodeficiency virus (HIV-1), those with compensated or decompensated cirrhosis, and those with HCV recurrence after liver transplant. Two phase 3 studies, AI444215 (ALLY-1) and AI444216 (ALLY-2), are provided in support of the proposed extension to the indication.

AI444215 was an open-label study with 2 parallel arms assessing the combination of DCV/SOF/RBV for 12 weeks in cirrhotic subjects who may require future liver transplantation and post-transplant subjects. The primary objectives of AI444215 were to demonstrate the SVR12 rate in genotype 1 infected cirrhotic subjects was greater than the composite estimated historical threshold of **41.6%** and to demonstrate the SVR12 rate in post-transplant genotype 1 infected subjects was greater than the historical threshold of **30%** achieved by pegIFN α /RBV. The SVR12 rate was defined as HCV RNA < LLOQ target detected (TD) or target not detected (TND) 12 weeks after the end of treatment.

A total of 113 subjects, 60 subjects in the cirrhotic cohort and 53 subjects in the post-liver transplant cohort were enrolled. In the cirrhotic cohort, the overall SVR12 rate was 83.3% (50/60, 95% CI: 71.5, 91.7), and the SVR12 rate in GT-1 infected subjects was 82.2% (37/45, 95% CI: 67.9, 92.0). The lower bound of the 95% CI, 67.9%, exceeded the 41.6% threshold. In the post-liver transplant cohort, the overall SVR12 rate was 94.3% (50/53, 95% CI: 84.3, 98.8) and the SVR12 rate in GT-1 infected subjects was 95.1% (39/41, 95% CI: 83.5, 99.4). The lower bound of the 95% CI, 83.5%, exceeded the 30% threshold. In the cirrhotic cohort, the SVR12 rates for GT-1 infected subjects were 90.9% (10/11, 95% CI: 58.6, 99.8) for those with Child-Pugh Score A (CPT A) at baseline, 91.7% (22/24, 95% CI: 73.0, 99.0) those with Child-Pugh Score B (CPT B) at baseline, and 50% (5/10, 95% CI: 18.7, 81.3) those with Child-Pugh Score C (CPT C) at baseline.

In conclusion, AI444215 demonstrated the efficacy of DCV/SOF/RBV for 12 weeks in HCV-1 infected subjects with compensated (CPT A) or decompensated (CPT B or CPT C) cirrhosis at baseline, and those with HCV recurrence after liver transplant. Chronic HCV-1 infected subjects with CPT C at baseline were limited in size and had a lower SVR12 rate compared to HCV genotype 1 subjects with CPT A or B. The optimal regimen for this subpopulation is uncertain and as such these statements are proposed for section 2 of the product label.

The primary objective of AI444216 was to demonstrate that the SVR12 rate in treatment-naive (TN) HCV genotype 1 subjects coinfecting with HIV who were treated with DCV and SOF therapy for 12 weeks was greater than the historical SVR rate of pegIFN α /RBV. The historical threshold achieved by PegIFN α /RBV was estimated at **29%** based on the results reported in the APRICOT study, in which 51 of 176 (29%) HCV genotype 1 subjects coinfecting with HIV achieved SVR24. A key secondary objective was to demonstrate that the SVR12 rate in treatment-experienced (TE) HCV GT-1 subjects coinfecting with HIV was greater than the

composite historical SVR. An estimated historical threshold of **5%** was proposed in the TE coinfection cohort since there are no approved treatments for this subpopulation.

AI444216 was an open-label, 3-arm, and 2-cohort study in HCV TN and HCV TE subjects coinfecting with HIV. The treatment-naïve subjects were randomized 2:1 to receive DCV/SOF combination for either 12 or 8 weeks. The treatment-experienced HCV/HIV coinfecting subjects who previously failed anti-HCV therapy received 12-weeks of combination DCV/SOF. A total of 203 subjects were treated: 101 TN subjects on the 12-week DCV/SOF regimen; 52 TE subjects on the 12-week DCV/SOF regimen; and 50 TN subjects on the 8-week DCV/SOF regimen.

For TN subjects who received 12-weeks of DCV/SOF, the overall SVR12 was 97.0% (98/101, 95% CI: 91.6, 99.4), and the SVR12 rate for GT-1 only was 96.4% (80/83, 95% CI: 89.8, 99.2). The lower bound of the 95% CI, 89.8%, was higher than the estimated historical rate of 29%. For TE subjects who received 12-week DCV/SOF, the overall SVR12 was 98.1% (51/52, 95% CI: 89.7, 100), and the SVR12 rate for GT-1 only was 97.7% (43/44, 95% CI: 88.0, 99.9). The lower bound of the 95% CI, 88.0%, was higher than the estimated historical rate of 5%. The SVR12 rates between TN and TE were comparable, and they are similar to the SVR12 rates of 12-weeks of Harvoni for HCV-1 mono-infected population in the Harvoni label.

For those who were TN HCV GT-1 coinfecting with HIV and treated with 12-weeks of DCV/SOF, the SVR12 rate was 89% (8/9, 95% CI: 51.8, 99.7) for subjects with cirrhosis at baseline, and the rate was 97% (72/74, 95% CI: 90.6, 99.7) for subjects without cirrhosis at baseline. For subjects who were TE HCV GT-1 co-infected with HIV and treated with 12-week of DCV/SOF, the SVR12 rate was 92% (12/13, 95% CI: 64.0, 99.8) for those with cirrhosis at baseline, and the rate was 100% (31/31, 95% CI: 88.8, 100) for those without cirrhosis at baseline.

The SVR rate was 90.9% (20/22, 95% CI: 70.8, 98.9) for HCV GT-1 HCV/HIV coinfecting TN and TE subjects with cirrhosis at baseline and treated with DCV/SOF for 12-weeks. The medical reviewer classified these patients as having compensated cirrhosis. A similar rate was observed in AI444215 in HCV GT-1 infected subjects with CPT A at baseline (i.e. compensated cirrhosis) and treated with DCV/SOF/RBV for 12-weeks. The 95% CIs overlapped with no evidence that the addition of RBV improves response rates, although the data is limited. Therefore, it seems reasonable to treat HCV GT-1 subjects with CPT A at baseline with DCV/SOF 12-weeks without RBV.

In study AI444216, 10 subjects who had HCV GT-3 coinfecting with HIV were enrolled and treated with 12-week of DCV/SOF. The SVR12 rate for TN group was 100% (6/6) with 95% CI of [69%, 100%] and 100% (4/4) with 95% CI of [40%, 100%] in TE group

In conclusion, Study AI444216 demonstrated the efficacy of DCV/SOF 12-weeks in GT-1 HCV/HIV coinfecting subjects either TN or TE.

Key statistical issues: None.

2. INTRODUCTION

This review evaluates an efficacy supplement from Bristol-Myers Squibb [BMS] to determine the efficacy of Daclatasvir.

2.1 Overview

Globally it is estimated that approximately 170 million people are infected with HCV, including approximately 3-5 million people in the United States (US) (<http://www.epidemic.org/thefacts/theepidemic/worldPrevalence/>). The most common HCV GT in the US is GT 1 (70-75%), followed by GT 2 and GT 3.

According to the clinical overview of the submission, in the current era of potent anti-HCV direct-acting antiviral agents (DAA) therapies, efficacy rates in HCV/HIV coinfecting subjects are comparable to those seen in HCV monoinfected subjects when treated with the newly approved DAA-containing regimens for ≥ 12 weeks.

Currently, SOF/RBV for 24 weeks has been approved for patients with GT-1, -3, and -4 chronic HCV infections, and this regimen may be shortened to 12 weeks in subjects with GT-2. Ombitasvir/paritaprevir plus dasabuvir \pm RBV for 12 to 24 weeks is approved for the treatment of HCV GT-1 infection only. In the HCV/HIV coinfecting population, there is little data in subjects with cirrhosis and subjects infected with non-GT-1 HCV.

Recurrence of HCV infection post-liver transplant can lead to accelerated allograft injury and fibrosis, and can significantly impair patient and graft survival. The approved all-oral HCV regimens that are indicated for use in HCV monoinfected patients with cirrhosis [Child-Pugh class A, B, or C], and patients with HCV recurrence post-liver transplant include SOF/RBV and ombitasvir/RTV-boosted paritaprevir/dasabuvir/RBV. SOF/RBV is only approved for subjects awaiting liver transplantation; SOF/RBV can be given up to 48 weeks or until liver transplantation, whichever comes first. The combination of ombitasvir/RTV-paritaprevir/dasabuvir + RBV for 24 weeks is only approved in post-liver transplant patients with GT-1 HCV who have normal hepatic function and mild fibrosis (Metavir fibrosis score ≤ 2); therefore, this regimen is not indicated for patients with advanced fibrosis or cirrhosis.

In this NDA submission, BMS proposes the use of DCV (Daklinza) in combination with sofosbuvir with or without ribavirin for the treatment of chronic HCV infected patients. The enrolled patients include those coinfecting with human immunodeficiency virus (HIV-1), those with compensated (CPT A) or decompensated (CPT B) cirrhosis, and those with HCV recurrence after liver transplant.

2.1.1 Study Reviewed

The detailed description of the study is listed in Table 1. Two phase 3 studies, AI444215 (ALLY-1) and AI444216 (ALLY-2), were submitted and reviewed in the efficacy supplement. All subjects enrolled in these two studies were from the US only.

Table 1 List of Phase 3 studies included in this review

Study	Phase and Design	Primary hypothesis	Treatment Period	# of Subjects per Arm	Study Population
AI444215 (Ally-1)	A Phase 3, open label, Genotype 1-6; Two cohorts: - Chronic Hepatitis C Infected subjects with Cirrhosis who may Require Future Liver Transplant and - Subjects Post-Liver Transplant	For cirrhotic cohort, the lower bound of the SVR12, 2-sided 95% CI will be used to compare to the composite historical threshold of 41.6% . For Post-Liver Transplant cohort, the lower bound of the SVR12, 2-sided 95% CI will be used to compare to the composite historical threshold of 30% .	DCV/SOF and Ribavirin (RBV) for 12 weeks	Cirrhotic cohort: (n=60) GT1-6 Enrolled 60 Post-Liver Transplant cohort: (n=50) GT1-6 Enrolled 53	Cirrhotic HCV infected and post-liver transplant
AI444216 (Ally-2)	A Phase 3, open label, Two cohorts: Treatment-naive (TN) and Treatment-experienced (TE) Chronic Hepatitis C (Genotype 1-6) Subjects coinfectd with Human Immunodeficiency Virus (HIV), Only 13 subjects with HCV-2, 3 subjects with HCV-4 and no subject with HCV-5 and -6.	For the primary objective, with 80 treatment-naive HCV/HIV-1 coinfectd, it would take a minimum of an observed SVR12 rate of 40% (32/80; 95% CI: 29.2%, 51.6%) for the lower bound of the 95% CI to exceed 29% . For the second key secondary objective, with 40 treatment-experienced HCV/HIV-1 coinfectd, it would take a minimum of an observed SVR12 rate of 15% (6/40; 95% CI: 5.7%, 29.8%) for the lower bound of the 95% CI to exceed 5% .	Daclatasvir (DCV) Plus Sofosbuvir (SOF) for 12 weeks	TN: (n=100) Enrolled 101 TE: (n=50); Enrolled 52 Total is 153 subjects enrolled One note: there was a third arm TN subjects treated with DCV/SOF for 8 weeks. Since the SVR12 was low and will be included in the label. 50 subjects enrolled into this arm.	HCV/HIV coinfectd subjects

The detailed design characteristics of the two phase 3 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 both studies AI444215 and AI444216. 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
 - Module 5- Clinical Study Reports (CSRs) of the Phase III Studies AI444215 and AI444216.

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

[\\CDSESUB1\evsprod\NDA206843\0052\m5\datasets\ai444215-ally-1\](#)
[\\CDSESUB1\evsprod\NDA206843\0052\m5\datasets\ai444216-ally-2\](#)

3. STATISTICAL EVALUATION

Studies AI444215 and AI444216 are reviewed under each of following sections. All tables and figures were generated by the statistical reviewer unless otherwise cited. For study AI444215, the cirrhotic cohort is abbreviated as “**Cirr**” and the post-liver transplant cohort is abbreviated as “**PostT**”. For study AI444216, the analyses are mainly focused on the 12 weeks of DCV/SOF groups. The treatment-naïve (TN) arm is abbreviated as “**TN**” and the treatment-experienced (TE) arm is abbreviated as “**TE**”. The 8 weeks of DCV/SOF TN arm is abbreviated as “**TN8**” in the summary tables in the appendix for reference purpose only.

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 datasets, EFF and VFAIL, for both Studies.

3.2 Evaluation of Efficacy

3.2.1 Study Design and Endpoints

❖ **AI444215 (ALLY-1), a phase 3 study for cirrhotic and post-liver transplant subjects:**

Title: A Phase 3 Evaluation of Daclatasvir, Sofosbuvir, and Ribavirin in Genotype 1-6 Chronic Hepatitis C Infection Subjects with Cirrhosis who may Require Future Liver Transplant and Subjects Post-Liver Transplant.

This was an open-label study with 2 parallel arms assessing the combination of DCV/SOF/RBV for 12 weeks in cirrhotic subjects who may require future liver transplantation and post-transplant subjects.

Males and females ≥ 18 years of age with HCV Genotype 1, 2, 3, 4, 5, or 6 infection and HCV

RNA \geq 10,000 IU/mL were eligible to enroll. The eligible subjects for the cirrhotic cohort are subjects with a MELD score of \geq 8 (and \leq 40). The eligible subjects for the post-transplant cohort are subjects who have received a liver transplant at least 3 months prior to screening.

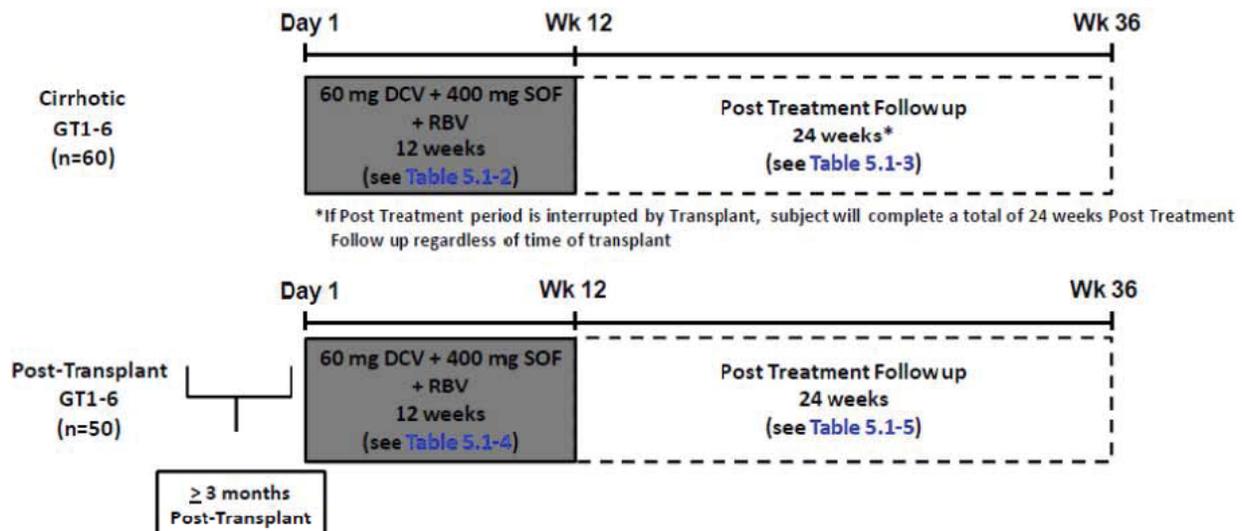


Figure 1: Study Diagram of AI444215 (copied from the protocol)

Research Hypothesis:

- In subjects with cirrhosis or in subjects post-liver transplant infected with HCV genotype 1, treatment with 12 weeks of DCV/SOF/RBV is safe and demonstrates SVR12 rates greater than the estimated historical threshold in subjects with cirrhosis and subjects who are post-liver transplant.

Primary Objectives:

- To demonstrate the SVR12 rate in genotype 1 infected cirrhotic subjects is greater than the composite estimated historical threshold. For the cirrhotic cohort, the lower bound of the SVR12, 2-sided 95% CI will be used to **compare to the composite historical threshold of 41.6%**.
- To demonstrate the SVR12 rate in post-transplant genotype 1 infected subjects is greater than the historical threshold achieved by pegIFN α /RBV. For the post-liver transplant cohort, the lower bound of the SVR12, 2-sided 95% CI will be used to **compare to the composite historical threshold of 30%**.

The historical thresholds used to assess the efficacy were previously reviewed and discussed during the development.

A). the cirrhotic cohort:

Using the results from Neutrino and HPC3007/C206 trials which were available at the time of submission, the composited historical threshold was calculated as the following:

Patient Profile	Proportion	SVR - Point Estimate	SVR – Upper Bound 95% CI	New Threshold	Proportion * New Threshold
<u>Child-Pugh A</u>					
Naïve	10%	81%	90%	90%	9.0%
Relapser	10%	73%	82%	82%	8.2%
Non-responder	10%	54%	73%	73%	7.3%
PI Failure	20%	54%	73%	73%	14.6%
<u>Child-Pugh B or C</u>	50%	Not Available		5%	2.5%
Overall Historical Threshold SVR rate					41.6%

Cited from the protocol in Appendix 4.

Based upon the proposed weighting, the historical threshold for SVR in Cirrhotic patients with the distribution described above was estimated at 41.6%. The composite of the population in the current trial had more null responders (19%) and more subjects with CPT B and C at baseline (76%) (Please see the demographic Table 17 in Appendix for GT-1 subjects for details). As a result, the re-calculated historical threshold based on these data will be lower than 41.6%. Since the SVR12 rate observed in the current trial was 82.2% with 95% CI of (67.9, 92.0), the lower bound of 95% CI 67.9% is much higher than 41.6%. It is not necessary to recalculate the new threshold here.

B). the post-liver transplant cohort:

Since pegIFN α /RBV results in sustained virologic responses (SVR) in up to 30% of treated patients with histological HCV recurrence after liver transplantation, the historical threshold for pegIFN α /RBV is estimated at 30%.

Sample Size:

There was no formal sample size calculation. With the target sample size of 48 GT-1 (out of 60 in total) cirrhotic subjects, the observed SVR12 rate can be estimated to 58% (28/48, 95% CI, 43.2%, 72.4%) for the lower bound of the 95% CI to exceed 41.6%. Similarly, with the target sample size of 40 GT-1 infected post-liver transplant subjects (out of 50 in total), it would take a minimum of an observed SVR12 rate of 48% (19/40, 95% CI, 31.5%, 63.9%) for the lower bound of the 95% CI to exceed 30%.

❖ AI444216 (ALLY-2), a phase 3 study for HCV/HIV coinfectd subjects:

Title: A Phase 3 Evaluation of Daclatasvir plus Sofosbuvir in Treatment-naïve and Treatment-experienced Chronic Hepatitis C (Genotype 1, 2, 3, 4, 5, or 6) Subjects Coinfected with Human Immunodeficiency Virus (HIV).

This was an open-label, 2-cohort, 3-arm study that planned to enroll approximately 200 HCV treatment-naïve and -experienced HCV subjects coinfectd with HIV. Approximately 150

treatment-naive subjects were randomized 2:1 (100:50) to receive DCV and SOF combination for either 12 weeks (arm 1: n ≈ 100 subjects) or 8 weeks (arm 2: n ≈ 50). Randomization was stratified by cirrhosis status (cirrhotic vs. non-cirrhotic) and HCV genotype. Subjects with genotype 1 HCV were further stratified by subtype (i.e. GT-1a, -1b). Additionally, approximately 50 HIV/HCV coinfecting subjects who previously failed anti-HCV therapy, received 12-weeks of combination DCV plus SOF (arm 3: n ≈ 50). See Figure 2 for the study design.

Subjects with compensated cirrhosis were eligible to enroll in the study. The proportion of cirrhotic subjects in each treatment cohort (HCV TN and TE) was capped at approximately 50%.

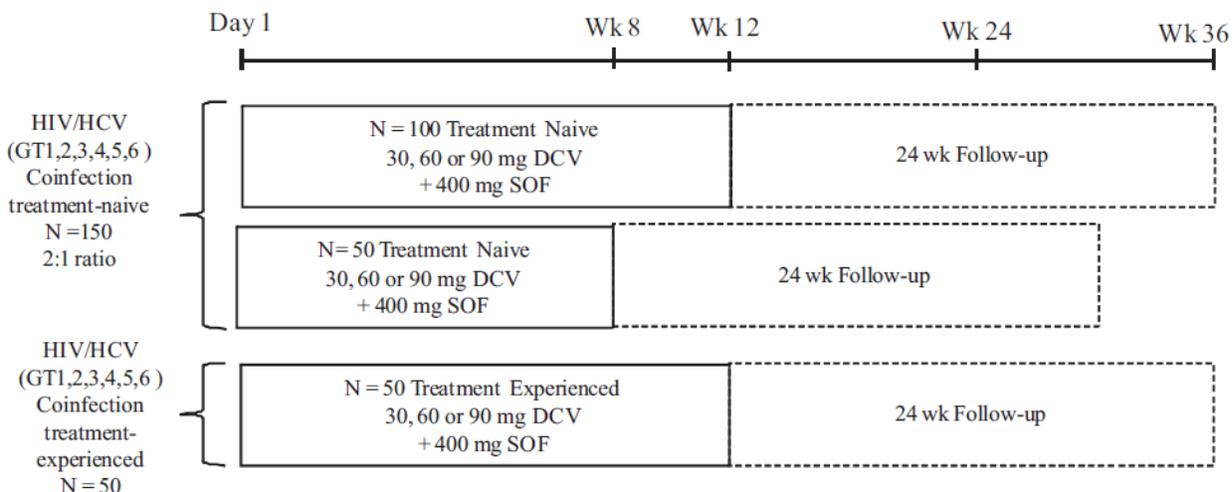


Figure 2: Study Diagram of AI444216 (copied from the protocol)

Research Hypothesis:

- Combination therapy with DCV and SOF for 12 weeks is safe and demonstrates an SVR12 rate greater than the historical rate of pegIFN α /RBV for the treatment of chronically-infected, treatment-naive HCV genotype1 subjects co-infected with HIV.

Primary Objective:

- To demonstrate the SVR12 rate in treatment-naive HCV genotype 1 subjects coinfecting with HIV who are treated with DCV and SOF therapy for 12 weeks is greater than the historical SVR rate of pegIFN α /RBV.

Key Secondary Objectives:

- To demonstrate the SVR12 rate for treatment-naive HCV genotype 1 subjects coinfecting with HIV on the DCV+SOE 8-week regimen, is greater than the historical SVR rate of pegIFN α /RBV. (*The SVR12 rate was very low and will not be included in the efficacy analyses.*)

- To demonstrate the SVR12 rate in treatment-experienced HCV genotype 1 subjects coinfecting with HIV is greater than the composite historical SVR rate.

The historical thresholds used to assess the efficacy were previously reviewed and discussed during drug development.

A). TN GT-1 cohort:

The historical threshold achieved by PegIFN α / RBV is estimated at **29%** based on the results reported in the APRICOT study, in which 51 of 176 (29%) HCV genotype 1 subjects coinfecting with HIV achieved SVR24.

B). TE GT-1 cohort:

There remains no approved treatment for subjects (monoinfected or coinfecting) that have failed previous PI add-on therapy. Therefore, an estimated historical threshold of **5%** is proposed in the treatment-experienced coinfection cohort.

These were the estimates at the time of the protocol review. The current thinking is that the HCV/HIV coinfecting population should have similar SVR12 rates with the DAA regimen. The new results from Harvoni label are as follows:

- For TN HCV GT-1 monoinfected non-cirrhotic subjects (Study ION-3), the SVR12 rate for 12 weeks Harvoni was 96% (208/216) with 95% CI ((b)(4)), or 99% (176/177) with 95% CI ((b)(4)) (observed in study ION-1).
- For TN HCV GT-1 monoinfected cirrhotic subjects (Study ION-1), the SVR12 rate for 12 weeks Harvoni was 94% (32/34) with 95% CI ((b)(4)).
- For TE HCV GT-1 monoinfected non-cirrhotic subjects (Study ION-2), the SVR12 rate for 12 weeks Harvoni was 94% (102/109) with 95% CI ((b)(4)).
- For TE HCV GT-1 monoinfected cirrhotic subjects (Study ION-2), the SVR12 rate for 24 weeks Harvoni was 99% (108/109) with 95% CI ((b)(4)).

Based on this, it is expected that the SVR12 rate from this regimen will be close to these estimates even though these SVR12 rates were from the HCV monoinfected populations.

Sample Size:

There was no formal sample size calculation. For the primary objective, with 80 treatment-naive HCV genotype 1 subjects co-infected with HIV, it would take a minimum of an observed SVR12 rate of 40% (32/80; 95% CI: 29.2%, 51.6%) for the lower bound of the 95% CI to exceed 29%. For TE GT-1 subpopulation, with 40 treatment-experienced HCV genotype 1 subjects coinfecting with HIV it would take a minimum of an observed SVR12 rate of 15% (6/40; 95% CI: 5.7%, 29.8%) for the lower bound of the 95% CI to exceed 5%.

The following sections are common for both studies.

Populations for Analyses:

- **Enrolled subjects** are those who signed an informed consent form and were assigned a Patient Identification Number (PID)
- **Treated subjects** are enrolled subjects who received at least 1 dose of study therapy.

Results were presented by cohort (Cirr or PostT in AI444215 and TN or TE in AI444216) 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.

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

Analysis Windows

Day 1 is the first dose of active study therapy. The general analysis windows are listed in Table 2 below.

Table 2 Analysis Windows for Phase 3 Studies

Study Period Label	Visit Label	Visit Number	Target Day from Start of Study Period	Visit Window
PRE-TREAT	PRE-TREAT	1	1	< 1 day ^a
ON-TREAT	DAY 1	2	1	1 - 4 days
	WEEK 1	3	7	5 days - 11 days
	WEEK 2	4	14	12 days - 3 weeks
	WEEK 4	5	28	> 3 weeks - 5 weeks
	WEEK 6	6	42	> 5 - 7 weeks
	WEEK 8	7	56	> 7 - 10 weeks
	WEEK 12	8	84	> 10 - 14 weeks
FOLLOW-UP	WEEK 12 EXT	9	140	> 14 weeks
	F/U WEEK 4	10	21	> 1 - 8 weeks
	F/U WEEK 12	11	77	> 8 - 18 weeks
	F/U WEEK 24	12	161	> 18 - 30 weeks
	F/U WEEK 24 EXT	13	245	> 30 weeks

Source: summarized from the Table 8.1-1 in the SAP for the study AI444215.

3.2.2 Patient Disposition, Demographic and Baseline Characteristics

3.2.2.1 Disposition

❖ Study AI44215

For study AI444215, a total of 116 were enrolled into the study, and 3 of them were not dosed and were excluded from the treated population. Table 3 describes the subject disposition of these treated subjects. The majority of treated subjects (96%) completed the designed 12-week treatment period and all of subjects completed the designed follow-up visits. Four subjects who did not complete the treatment and were classified as other in the cirrhotic cohort had a liver transplant during the trial (AI444215-1-50, AI444215-3-17, AI444215-3-100, and AI444215-3-104), and all of them met SVR12. One subject (AI444215-3-116) discontinued the treatment due to AE in post-liver transplant cohort also met SVR12.

Table 3: Subjects Disposition for Study AI444215 (Treated Subjects)

Subgroup	Cirr	PostT	Total
N	60	53	113
Completed Treatment Period			
YES	56 (93.3%)	52 (98.1%)	108 (95.6%)
NO	4 (6.7%)	1 (1.9%)	5 (4.4%)
Reasons of NOT completed treatment			
ADVERSE EVENT	. (. %)	1 (1.9%)	1 (0.9%)
OTHER	4 (6.7%)	. (. %)	4 (3.5%)
Completed Follow-Up			
YES	60 (100.0%)	53 (100.0%)	113 (100.0%)

❖ Study AI44216

A total of 153 subjects were enrolled into 12 weeks of treatment. Table 4 describes the subject disposition of these treated subjects. Almost all treated subjects (99%) completed the designed 12-week treatment period and completed the designed follow-up period. Only one subject (AI444216-19-138) stopped the drug after 6 weeks and did not finish the follow-up period in TN group.

Table 4: Subjects Disposition for Study AI444216 (Treated Subjects)

Subgroup	TN	TE	Total
N	101	52	153
Completed Treatment Period			
YES	99 (98.0%)	52 (100.0%)	151 (98.7%)
NO	2 (2.0%)	. (. %)	2 (1.3%)
Reasons of NOT completed treatment			
OTHER	1 (1.0%)	. (. %)	1 (0.7%)
POOR/NON-COMPLIANCE	1 (1.0%)	. (. %)	1 (0.7%)
Completed Follow-Up			
YES	100 (99.0%)	52 (100.0%)	152 (99.3%)
NO	1 (1.0%)	. (. %)	1 (0.7%)

3.2.2.3 Demographic and Baseline Characteristics

❖ Study AI44215

Baseline demographics were generally comparable in the cirrhotic and post-liver transplant cohorts. More than half of the subjects were male (67.3%). Overall, the mean age was 58.7 years with 18.6% of subjects ≥ 65 years of age. Most subjects were white (95.6%) and a small proportion were black/African American (3.5%) or Asian (0.9%). Most subjects had HCV GT-1 (76.1%): GT-1a (57.5%) and GT-1b (18.6%). The mean HCV RNA level was 6.0 log₁₀ IU/mL in the cirrhotic cohort and was 6.6 log₁₀ IU/mL in the post-liver transplant cohort. More than half of subjects in the cirrhotic cohort (55.0%) had a baseline viral load $\geq 800,000$ IU/mL and 88.7% of subjects in the post-liver transplant cohort had baseline viral load $\geq 800,000$ IU/mL. In the cirrhotic cohort, 20.0% of subjects had a Child-Pugh Score (CPT) A at baseline, 53.3% had CPT B and 26.7% had CPT C. Please see Table 16 in the Appendix for details.

❖ Study AI44216

Between TN and TE subjects who received 12 weeks of treatment, baseline demographics were generally comparable. Most of the subjects were male (88.2%). Overall, the mean age was 52.0 years with only 5.2% of subjects ≥ 65 years of age. More than half of subjects were white (63.4%) and 32.7% were black. Most subjects had HCV GT-1 (83.0%): GT-1a (68.0%) and GT-1b (15.0%). The mean HCV RNA level was 6.5 log₁₀ IU/mL and 80.4% of subjects had a baseline viral load $\geq 800,000$ IU/mL. A small proportion of subjects had cirrhosis at baseline, 8.9% in TN group and 28.8% in the TE group. Please see Table 18 in the Appendix for details.

The baseline demographics for TN8 group were listed in Table 19 in the Appendix for reference only.

3.2.3 Statistical Methodologies

Ninety-five percent (95%) CIs were calculated for the SVR rates for each cohort separately within the study. Binary antiviral activity endpoints were assessed by the applicant using the treated population.

3.2.4 Results and Conclusions

3.2.4.1 Summary of Applicant's Results

❖ Study AI44215

Overall SVR₁₂ rates were 83.3% in cirrhotic subjects and 94.3% in post-liver transplant subjects (Table 5). For GT-1 subjects, SVR₁₂ rates were 82.2% in cirrhotic subjects and 95.1% in post-liver transplant subjects (Table 5).

Note that there were 2 subjects who had SVR12=0 (failure) in the CSR were later found to be cured and were imputed as SVR12=1 (success). The details are as follows.

- Subject [AI444215-1-50](#) had a liver transplant on Day 71 and then had 12 weeks of treatment extension. When the database locked, SVR8=1 was observed. As a result, the CSR reported SVR12=0 (failure). Subsequently, the subject was found to have SVR12=1, and was treated as a success in the ISE. (62 white GT-3, Child-Pugh score 13 (CPT C), MELD=24, with treatment extension).
- Subject [AI444215-3-100](#) had a liver transplant on Day 23 at another medical center. The subject left the trial without HCV RNA VL data. So, the SVR12=0 (failure) in the CSR. Subsequently, the subject was found to have SVR24=1, and was treated as a success in the ISE. (58 white GT-4, Child-Pugh score 11 (CPT C), MELD=21, without treatment extension).

Some subgroup analyses results are listed in Table 5 (by genotype) and Table 6. Mean HCV RNA changes from baseline in Study AI444215 for treated subjects measured in log10 IU/mL are shown in Figure 3 below.

Table 5: Applicant's SVR12 Results for Study AI444215 (Treated Subjects)

Table 4.4.2-1: ALLY-1 Efficacy Results with 12 Weeks of DCV/SOF/RBV in Cirrhotic and Post-Transplant Subjects: All Treated Subjects

Virologic Endpoints Responder (%)	Post-Transplant (N = 53)	Cirrhosis (Child-Pugh class A, B, or C) (N = 60)
SVR12 ^a		
GT-1 Subjects	39/41 (95.1) 95% CI (83.5, 99.4)	37/45 (82.2) 95% CI (67.9, 92.0)
GT-1a	30/31 (96.8)	26/34 (76.5)
GT-1b	9/10 (90.0)	11/11 (100.0)
All Genotypes (includes GT-1)	50 (94.3)	50 (83.3) ^d
GT-2	-	4/5 (80.0)
GT-3	10/11 (90.9)	5/6 (83.3) ^d
GT-4	-	4/4 (100.0) ^d
GT-6	1/1 (100.0)	-
Virologic Failure (all genotypes)	3/53 (5.7)	10/60 (16.7)
On-Treatment Failure ^b	0	1/60 (1.7)
Failure During Follow-up		
Relapse ^c	3/53 (5.7)	9/58 (15.5)

SVR12: HCV RNA < LLOQ, TD or TND

*Primary endpoint: SVR12 in GT-1 subjects

a For SVR12 only, missing HCV RNA data at follow-up Week 12 were imputed using the Next Value Carried Backwards (NVCB) approach. For subjects who missed the follow-up Week 12 visit, SVR12 was imputed using the next and closest available HCV RNA measurement after the follow-up Week 12 window.

b There were no cases of virologic breakthrough. Includes non-responders with missing or detectable HCV RNA at end of treatment.

c Rates were computed among all subjects with HCV RNA < LLOQ, TND at end of treatment.

d Two cirrhotic subjects with missing HCV RNA at follow-up Week 12 achieved SVR after database lock for the clinical study report. With the addition of these subjects, this SVR12 rate is 83.3% (50/60) for the cirrhotic cohort (all genotypes). One subject (GT-4) went to another center for transplant at Week 3 and subsequently achieved SVR24 (imputed SVR12), 6 months after transplant without additional HCV therapy. The other subject (GT-3) had transplant/treatment extension and subsequently achieved SVR12.

Source: Module 2.5 Clinical Overview, Table 4.4.2-1.

Table 6: Applicant’s SVR12 Subgroup Analyses by Baseline Cirrhosis for Study AI444215 (Treated Subjects)

Table 7.3.4-2: SVR12 by Baseline Subgroups of Cirrhotic Subjects (All Genotypes): Treated Subjects

Parameter ^a	n/N (%)
Child-Pugh Class	
A	11/12 (91.7)
B	30/32 (93.8)
C	7/16 (43.8)
MELD Score	
< Median at baseline	26/29 (89.7)
≥ Median at baseline	22/31 (71.0)
< 15	34/39 (87.2)
≥ 15	14/21 (66.7)

^a This table does not include the 2 cirrhotic subjects with missing HCV RNA at follow-up Week 12, who achieved SVR after database lock for the clinical study report: AI444215-3-100 with GT-4 and AI444215-1-50 with GT-3.
 Source: study AI444215 CSR, Table 7.3.4-2

Figure 7.3.1-1: Mean (95% CI) HCV RNA log₁₀: Treated Subjects

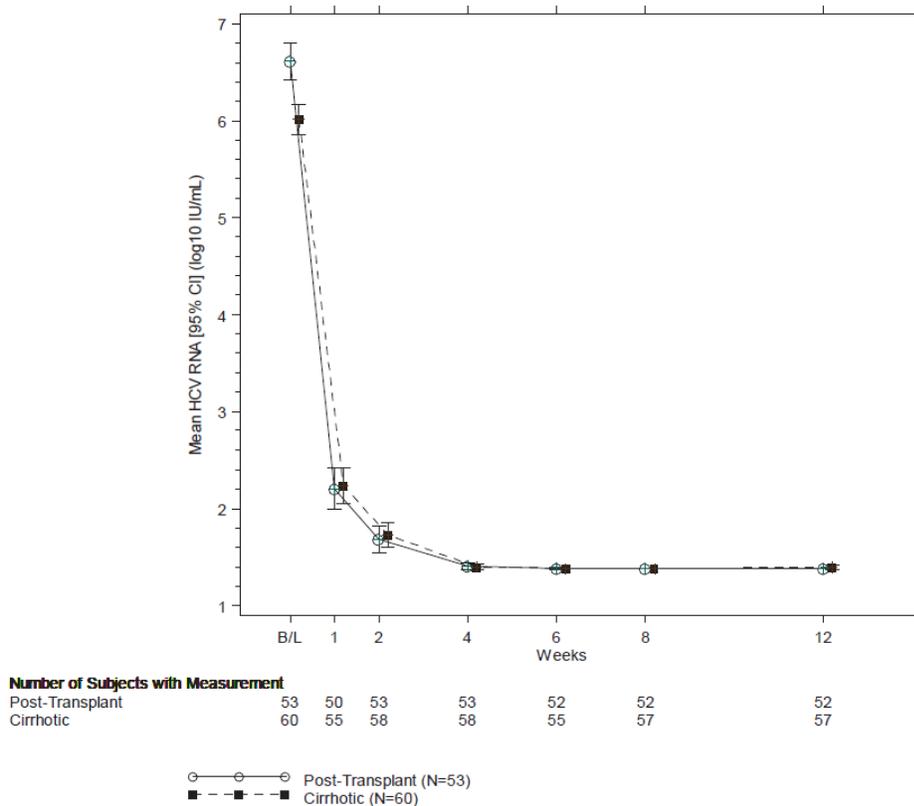


Figure 3: Mean HCV RNA Change from Baseline for Study AI444215 (Observed Values for Treated Subjects) Source: study AI444215 CSR, Figure 7.3.1-1.

❖ Study AI44216

Overall SVR12 rates were 97.0% in TN subjects and 98.0% in TE subjects who received 12 weeks of DCV/SOF treatment (Table 7). For GT-1 subjects, SVR12 rates were 96.4% in TN subjects and 97.7% in TE subjects who received 12 weeks of DCV/SOF treatment (Table 7). The SVR12 rate for TN subjects who only received 8 weeks of DCV/SOF treatment was 76.0% overall, and the reviewer will not discuss this result except in the summary tables in the Appendix for reference only.

Some subgroup analyses results (by genotype) are listed in Table 7 and Table 8. Mean HCV RNA changes from baseline in study AI444216 for treated subjects measured in log₁₀ IU/mL are shown in Figure 4 below.

Table 7: Applicant's SVR12 Results for Study AI444216 (Treated Subjects)

Table 4.4.1-1: ALLY-2 Efficacy Results with 8 or 12 Weeks of DCV/SOF in HCV/HIV Coinfected Subjects: All Treated Subjects

Virologic Endpoints Responder (%)	HCV	HCV	HCV
	Treatment-Naive 12 Weeks DCV/SOF	Treatment-Experienced 12 Weeks DCV/SOF	Treatment-Naive 8 Weeks DCV/SOF
SVR12^a			
GT-1 Subjects	80/83 (96.4)* 95% CI (89.8, 99.2)	43/44 (97.7) 95% CI (88.0, 99.9)	31/41 (75.6) 95% CI (59.7, 87.6)
GT-1a	68/71 (95.8)	32/33 (97.0)	28/35 (80.0)
GT-1b	12/12 (100.0)	11/11 (100.0)	3/6 (50.0)
All Genotypes (includes GT-1)	98/101 (97.0) 95% CI (91.6, 99.4)	51/52 (98.0) 95% CI (89.7, 100.0)	38/50 (76.0) 95% CI (61.8, 86.9)
GT-2	11/11 (100.0)	2/2 (100.0)	5/6 (83.3)
GT-3	6/6 (100.0)	4/4 (100.0)	2/3 (66.7)
GT-4	1/1 (100.0)	2/2 (100.0)	-
Virologic Failure			
All Genotypes (includes GT-1)	3/101 (3.0)	1/52 (1.9)	12/50 (24.0)
On-Treatment Failure ^b	1/101 (1.0) ^b	0	0
Failure During Follow-up			
Relapse ^c	1/100 (1.0)	1/52 (1.9)	10/50 (20.0)
Other ^d	1/100 (1.0)	0	2/50 (4.0)

SVR12: HCV RNA < LLOQ, TD or TND

*Primary endpoint: SVR12 in treatment-naive GT-1 subjects that received 12 weeks of DCV/SOF

a For SVR12 only, missing HCV RNA data at follow-up Week 12 were imputed using the Next Value Carried Backwards (NVCB) approach. For subjects who missed the follow-up Week 12 visit, SVR12 was imputed using the next and closest available HCV RNA measurement after the follow-up Week 12 window.

b This subject was non-compliant, discontinued early, and had detectable HCV RNA at EOT.

c Rates were computed among all subjects with HCV RNA < LLOQ, TND at EOT.

d Includes subjects with HCV RNA < LLOQ, TND at EOT, but who had missing HCV RNA at follow-up Week 12 and subsequent time points.

Source: Module 2.5 Clinical Overview, Table 4.4.1-1.

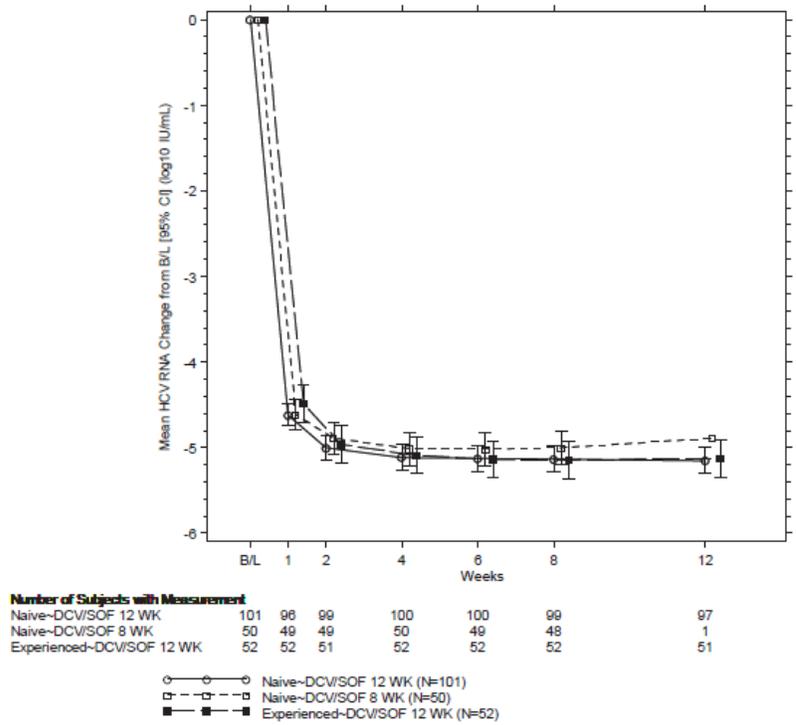
Table 8: Applicant's SVR12 Subgroup Analyses by Baseline Cirrhosis for Study AI444216 (Treated Subjects)

Table 4: Summary of Sustained Virologic Response (< LLOQ [TD or TND]) at Follow-up Week 12 (SVR12) by Subgroup: All HCV/HIV Coinfected Subjects

Subgroup Analysis	Subjects with HCV RNA, Responder/Evaluable (Percent)		
	Naive DCV/SOF 12 Week (N = 101)	Naive DCV/SOF 8 Week (N = 50)	Experienced DCV/SOF 12 Week (N = 52)
Gender			
Male	90/92 (97.8)	33/42 (78.6)	42/43 (97.7)
Female	8/9 (88.9)	5/8 (62.5)	9/9 (100)
Age Category (years)			
< 65	93/96 (96.9)	36/47 (76.6)	48/49 (98.0)
≥ 65	5/5 (100)	2/3 (66.7)	3/3 (100)
Race			
White/Caucasian	63/66 (95.5)	20/28 (71.4)	31/31 (100)
Black/AA	30/30 (100)	15/19 (78.9)	19/20 (95.0)
Asian	1/1 (100)	1/1 (100)	--
Other	4/4 (100)	2/2 (100)	1/1 (100)
Baseline HCV RNA (IU/mL)			
< 800,000	22/22 (100)	6/6 (100)	8/8 (100)
≥ 800,000	76/79 (96.2)	32/44 (72.7)	43/44 (97.7)
< 2,000,000	33/35 (94.3)	18/18 (100)	17/17 (100)
≥ 2,000,000	65/66 (98.5)	20/32 (62.5)	34/35 (97.1)
< 6,000,000	56/58 (96.6)	27/34 (79.4)	33/33 (100)
≥ 6,000,000	42/43 (97.7)	11/16 (68.8)	18/19 (94.7)
Baseline Cirrhosis			
Absent	88/90 (97.8)	34/44 (77.3)	34/34 (100)
Present	8/9 (88.9)	3/5 (60.0)	14/15 (93.3)
Not reported	2/2 (100)	1/1 (100)	3/3 (100)
Baseline IL-28B Genotype (SNP rs12979860)			
CC	28/28 (100)	9/13 (69.2)	13/13 (100)
Non-CC (CT and TT)	70/73 (95.9)	29/37 (78.4)	38/39 (97.4)

Source: study AI444216 CSR, Table 4

Figure 7.3.3-1: Mean (95% CI) Decline from Baseline in log₁₀ HCV RNA - Treated Subjects



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Note: One subject (AI444216-7-124) in the treatment-naive 8-week DCV/SOF group is recorded in the database as not transitioning to the post-treatment period after 8 weeks. This is due to a clerical error, which will be corrected in an addendum to this CSR. See Section 4.2.

Figure 4: Mean HCV RNA Change from Baseline for Study AI444216 (Observed Values for Treated Subjects) Source: study AI444216 CSR, Figure 7.3.1-1.

3.2.4.2 Study AI444215 (ALLY-1) Primary Efficacy Results

➤ **Primary Efficacy Analysis Results**

The pre-specified primary efficacy endpoint for this study was SVR12 for GT-1 subjects only. The statistical reviewer obtained the same SVR12 (<LOQ) results as the applicant. Overall, the SVR12 rate was 88.4% (Table 9 and Figure 5). The SVR12 rates in both cohorts were 82.2% in cirrhotic subjects and 95.1% in post-liver transplant subjects, and both exceeded the pre-specified historical thresholds. The relapse rates were 15.9% in cirrhotic subjects and 4.9% in post-liver transplant subjects. One subject in the cirrhotic cohort had detectable HCV at end-of-treatment (EOT) then virologic relapse.

Table 9: SVR12 and Virologic Failure Rates for GT-1 Subjects Only in Study AI444215 (Treated Subjects)

Cohort	Cirr N=45	PostT N=41	Total N=86
Responder (SVR12) 95% CI	37 (82.2%) (67.9%, 92.0%)	39 (95.1%) (83.5%, 99.4%)	76 (88.4%) (79.7%, 94.3%)
Failure	8 (17.8%)	2 (4.9%)	10 (11.6%)
Reasons of Virologic Failure			
DETECTABLE HCV at EOT	1 (2.2%)	. (. %)	1 (1.2%)
Relapse rate*	7/44 (15.9%)	2/41 (4.9%)	9/85 (10.6%)

*: Relapse rates were calculated with a denominator of subjects with undetectable HCV RNA at the end of treatment (EOT).

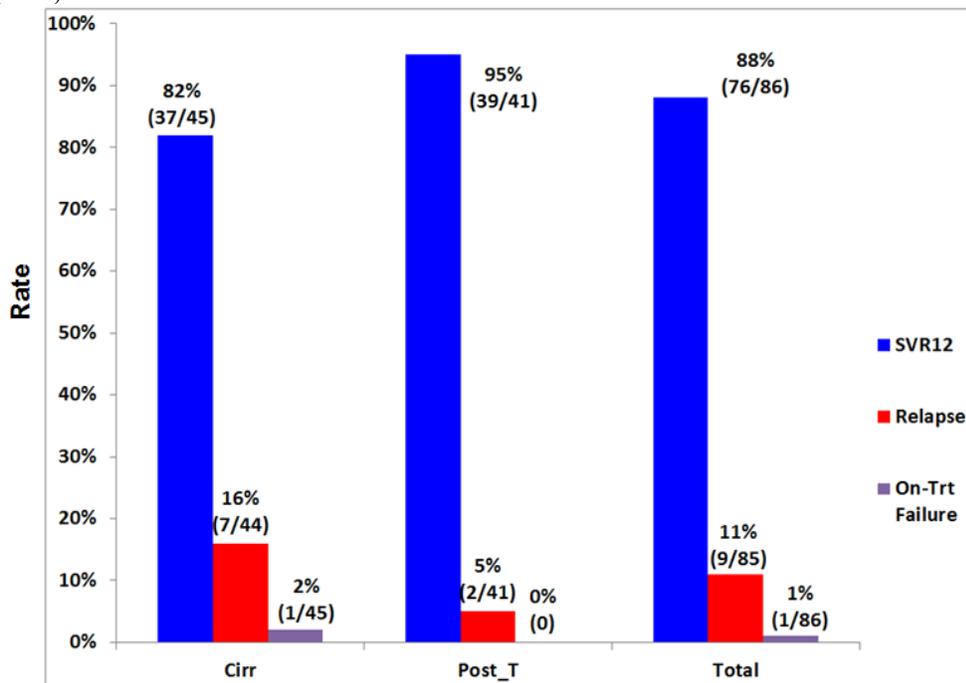


Figure 5: Study AI444215 SVR12, Relapse, On-Treatment Failure for GT-1 Subjects Only (Treated Subjects)

➤ Secondary Efficacy Analysis Results

For the cirrhotic cohort, the overall SVR12 rate was 83.3% (50/60, 95% CI: 71.5, 91.7) and the overall SVR12 rate was 94.3% (50/53, 95% CI: 84.3, 98.8) for post-liver transplant cohort (Table 10 and Figure 6). These results are the same as the CSR reported. The imputation of one subject to SVR12=success did not change the SVR12 rate (from 82.2% to 81.7%) (Table10).

About half of subjects had viral suppression at Week 4 and almost all of them had viral suppression at Week 8 (Figure 7). The suppression rates at different time points were listed in Table 20 and 21 in Appendix.

Table 10: SVR12 and Virologic Failure Rates for All Subjects in Study AI444215 (Treated Subjects)

Cohort	Cirr N=60	PostT N=53	Total N=113
Responder (SVR12) 95% CI	50 (83.3%) (71.5%, 91.7%)	50 (94.3%) (84.3%, 98.8%)	100 (88.5%) (81.1%,93.7%)
Failure	10 (16.7%)	3 (5.7%)	13 (11.5%)
Reasons of Virologic Failure			
DETECTABLE HCV at EOT	1 (1.7%)	. (. %)	1 (0.9%)
Relapse rate*	9/58 (15.5%)	3/53 (5.7%)	12/111 (10.8%)
--- No imputation for AI444215-3-100 (only had SVR24=1 available) ---			
Success	49 (81.7%)	50 (94.3%)	99 (87.6%)
Reasons of Virologic Failure			
DETECTABLE HCV at EOT	2 (3.3%)	. (. %)	2 (1.8%)
RELAPSE	9/58 (15.5%)	3/53 (5.7%)	12/111 (10.8%)

*: Relapse rates were calculated with a denominator of subjects with undetectable HCV RNA at the end of treatment (EOT).

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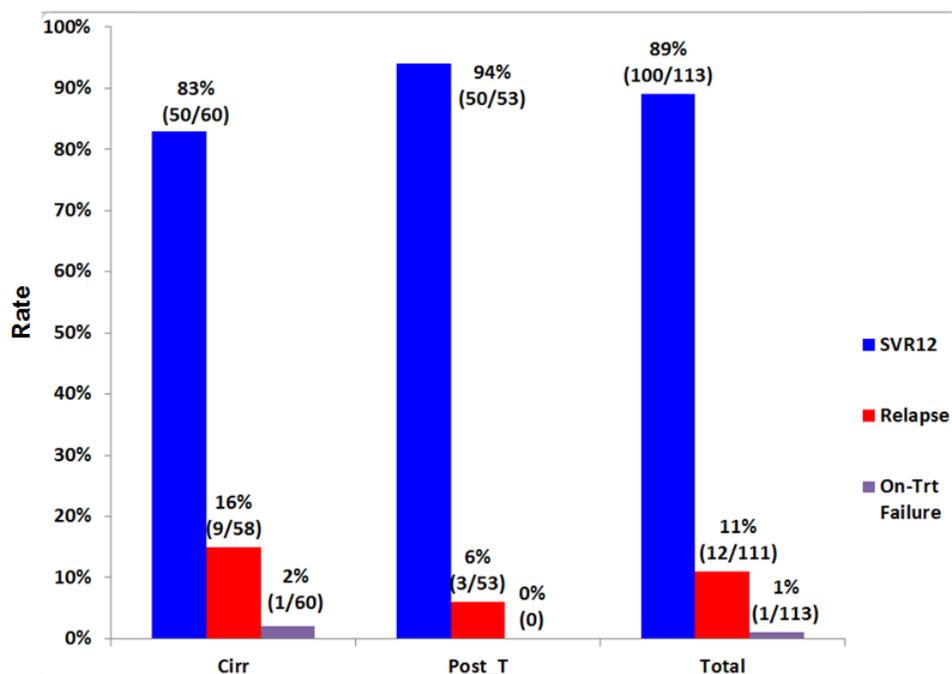


Figure 6: Study AI444215 SVR12, Relapse, On-Treatment Failure for All Subjects (Treated Subjects)

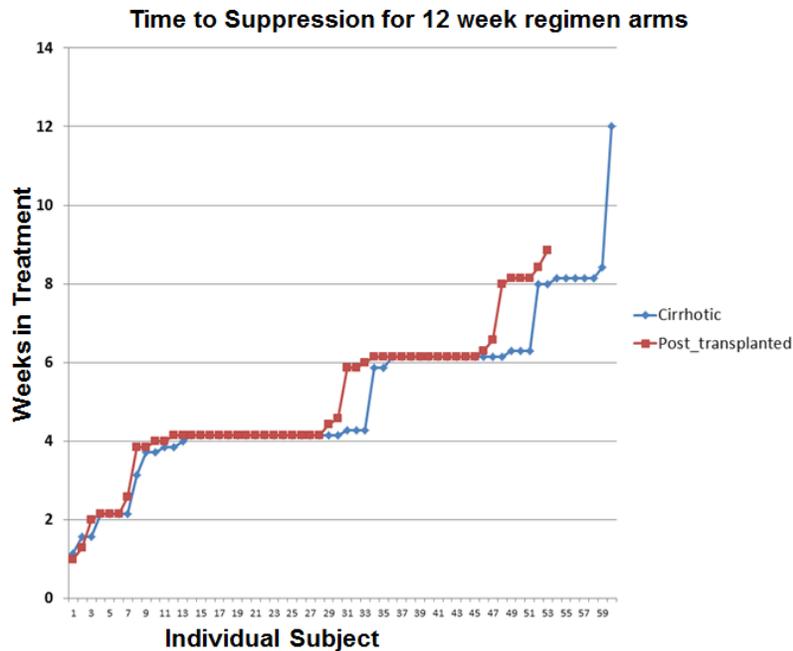


Figure 7: Study AI444215 Time to Suppression for All Subjects (Treated Subjects)

➤ **MELD Score Improvement**

For the cirrhotic cohort, subjects’ MELD score changes at follow-up 12 weeks from baseline were calculated. For subjects who had SVR12=success, the MELD score changes could be within ± 3 range for subjects who had MELD score < 15 at baseline. While if the subjects’ MELD score is ≥ 15 at baseline, a slightly higher proportion of subjects had improved (decreased) MELD scores (Figure 8). This seems to indicate that the follow-up 12-weeks after EOT is too short to observe significant MELD score improvement from baseline.

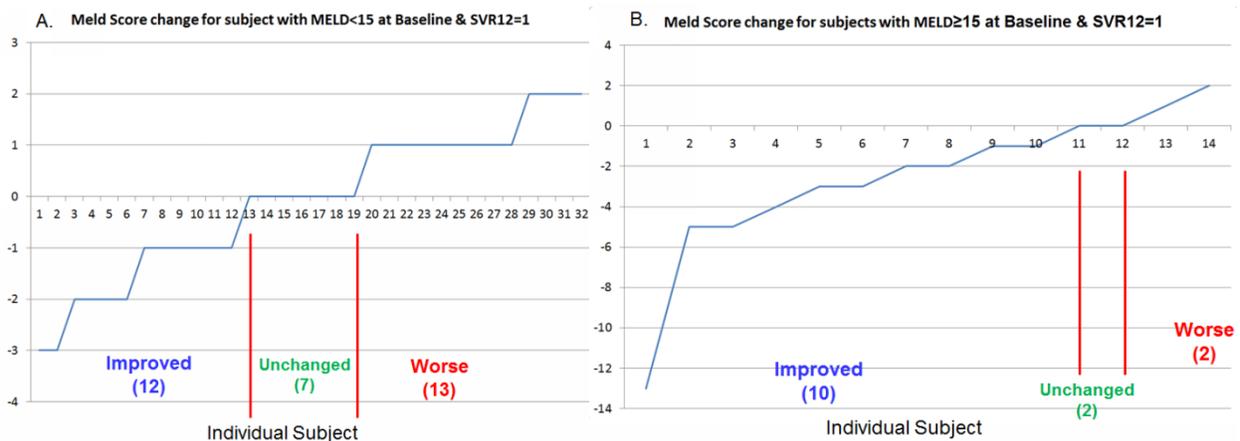


Figure 8: Study AI444215 MELD Score Changes at FU-12 from Baseline for Subjects who Had SVR12=Success in Cirrhotic Cohort (A: subjects had MELD < 15 at baseline; B: subjects had MELD ≥ 15 at baseline)

For subjects who failed at SVR12, their MELD score changes at FU-12 from baseline could be increased or decreased (Figure 9).

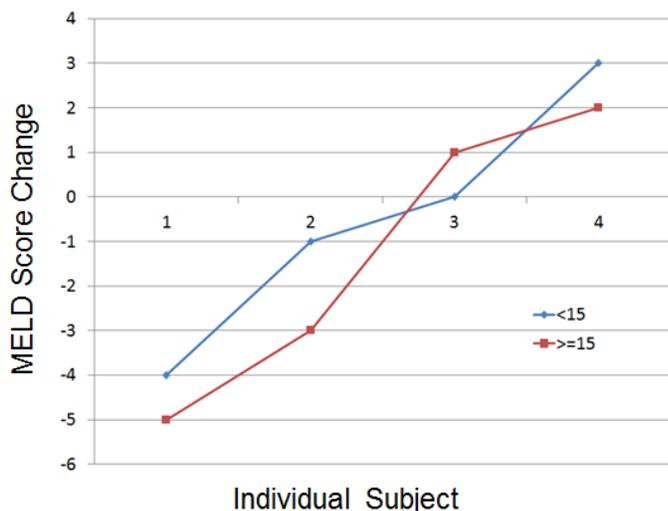


Figure 9: Study AI444215 MELD Score Changes at FU-12 from Baseline for Subjects who Had SVR12=Failure in Cirrhotic Cohort

3.2.4.3 Study AI444216 Primary Efficacy Results

Only subjects who received 12 weeks of treatment were included in the efficacy analyses. .

➤ Primary Efficacy Analysis Results

The pre-specified primary efficacy endpoint for this study was SVR12 for TN GT-1 subjects only. The statistical reviewer obtained the same SVR12 (<LOQ) results as the applicant. The SVR12 rates were 96.4% in TN GT-1 subjects and 97.7% in TE GT-1 subjects, and both exceeded the pre-specified historical thresholds (Table 11 and Figure 10). The SVR12 rates were comparable between TN and TE groups. The combined SVR12 rate of 96.9% in HCV-1/HIV coinfecting subjects is also comparable to the SVR12 rates of 12-weeks of Harvoni treatment in the HCV GT-1 mono-infected subpopulation in the Harvoni label.

The relapse rates were 2.4% in TN subjects and 2.3% in TE subjects. One subject (AI444216-19-138) in TN cohort who missed Follow-up Week 12 visit and had suppression at EOT visit was counted as a relapser here even though the applicant counted it as missing data instead of a relapser. One subject in the TN cohort had detectable HCV at EOT.

Table 11: SVR12 and Virologic Failure Rates for GT-1 Subjects Only in Study AI444216 (Treated Subjects)

Cohort	TN N=83	TE N=44	Total N=127
Responder (SVR12) 95% CI	80 (96.4%) (89.8%, 99.3%)	43 (97.7%) (88.0%, 100%)	123 (96.9%) (92.1%, 99.1%)
Failure	3 (3.6%)	1 (2.3%)	4 (3.1%)
Reasons of Virologic Failure			
DETECTABLE HCV RNA at EOT	1 (1.2%)	. (. %)	1 (0.8%)
Relapse Rate*	2/82 (2.4%)	1/44 (2.3%)	3/126 (2.4%)

*: Relapse rates were calculated with a denominator of subjects with undetectable HCV RNA at the end of treatment (EOT).

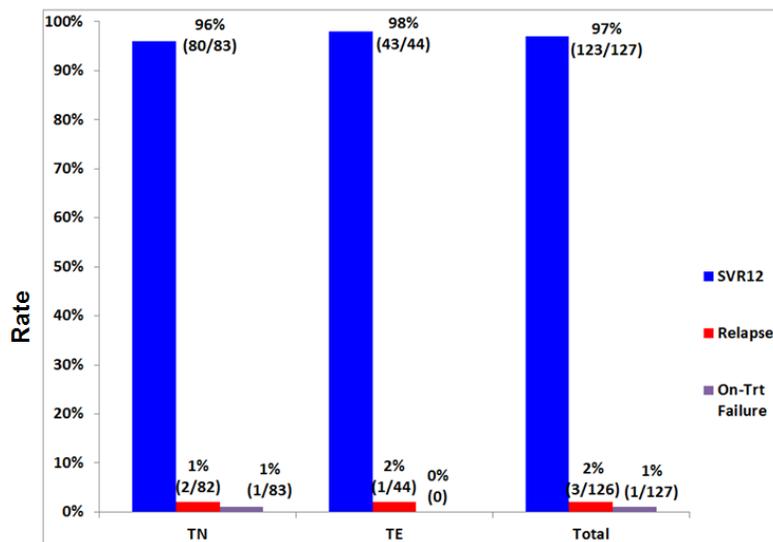


Figure 10: Study AI444216 SVR12, Relapse, On-Treatment Failure for GT-1 Subjects Only (Treated Subjects)

➤ Secondary Efficacy Analysis Results

For the TN group with 12 weeks of treatment, the overall SVR12 rate was 97.0% (98/101, 95% CI: 91.6, 99.4), and the overall SVR12 rate was 98.1% (51/52, 95% CI: 89.7, 100) for the TE group with 12 weeks of treatment (Table 12 and Figure 11). These results are the same as the CSR reported. The SVR12 rate for TN 8 weeks of treatment is listed here for reference only.

One subject (AI444216-16-141 with GT-2) in TN group had SVR12=success while SVR24=failure, ie, a relapser and it was not counted here.

More than half of subjects had viral suppression at Week 4 and almost all of them had viral suppression at Week 8 (Figure 12). The suppression rates at different time points were listed in Table 22 (GT-1 only), Table 23 (GT-1 and -3), and Table 24 (Overall) in the Appendix

Table 12: SVR12 and Virologic Failure Rates for All Subjects in Study AI444216 (Treated Subjects)

Cohort	TN N=101	TE N=52	TN8 N=50
Responder (SVR12) 95% CI	98 (97.0%) (91.6%, 99.4%)	51 (98.1%) (89.7%, 100%)	38 (76.0%) (61.8%, 86.9%)
Failure	3 (3.0%)	1 (1.9%)	12 (24.0%)
Reasons of Virologic Failure			
DETECTABLE HCV at EOT	1 (1.0%)	. (. %)	. (. %)
Relapse rate*	2/100 (2.0%)	1/52 (1.9%)	12/50 (24.0%)

*: Relapse rates were calculated with a denominator of subjects with undetectable HCV RNA at the end of treatment (EOT).

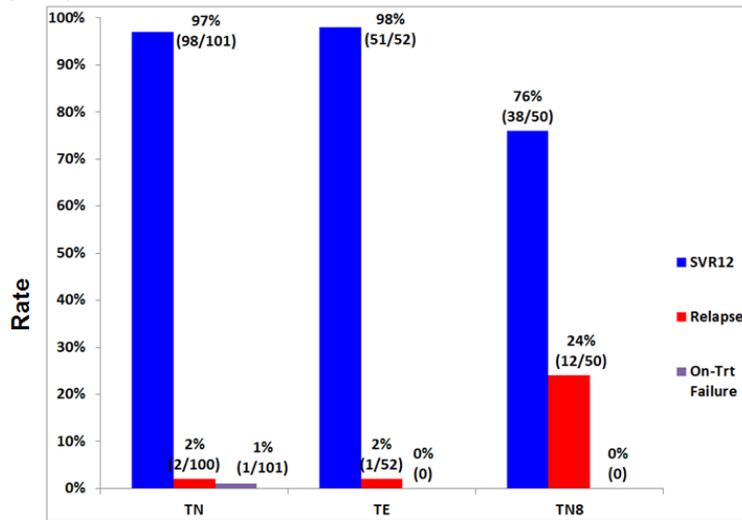


Figure 11: Study AI444216 SVR12, Relapse, On-Treatment Failure for All Subjects (Treated Subjects)
Time to Suppression for 12 week regimen arms

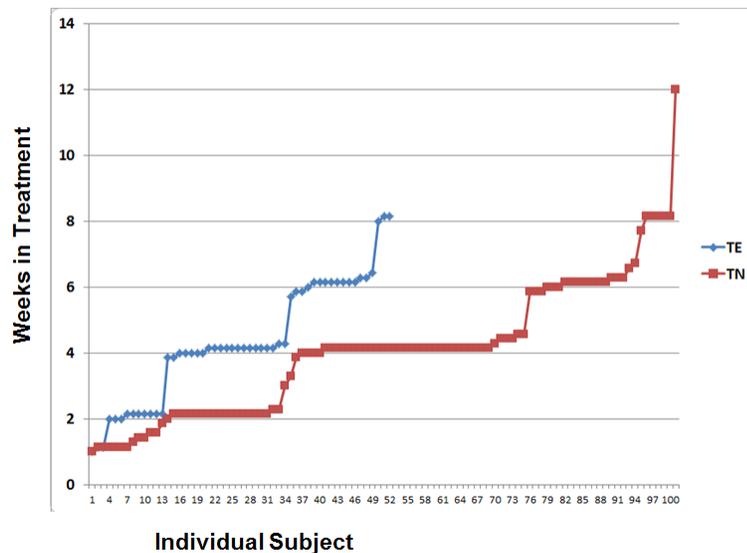


Figure 12: Study AI444216 Time to Suppression for All Subjects with 12-Weeks of Treatment (Treated Subjects)

3.2.4.4 Comparison of GT-1 CPT A Cirrhosis Subjects between AI444215 and AI444216

When comparing the two studies, we noticed that monoinfected HCV GT-1 subjects with CPT A at baseline who received DCV/SOF/RBV for 12-weeks in AI444215 had SVR12=90.9% (10/11, 95% CI: 58.6, 99.8). While GT-1 HCV/HIV coinfecting subjects with cirrhosis at baseline (which is the same as CPT A at baseline as the medical reviewer indicated) who received DCV/SOF for 12-weeks in AI444216 had SVR12=90.9% (20/22, 95% CI: 70.8, 98.9) (Table 13). Since the 95% CIs of two SVR12 rates overlapped, it is reasonable to treat HCV GT-1 subjects with CPT A at baseline with DCV/SOF 12-weeks without RBV. Similar SVR12 rates were observed for all enrolled as well (Table 13).

When GT-1 CPT A subjects were analyzed by treatment history (TN vs. TE), there were numeric differences between the two regimens within the TN and TE groups. The trends were not the same. This may be due to the small sample size (Figure 13).

Table 13: SVR12 for Subjects with CPT A at Baseline in Studies AI444215 and AI444216 (Treated Subjects)

Child-Pugh Class A		Overall (TN+TE)	
	SVR12	AI444215 (Ally-1) (DCV/SOF 12-weeks)	AI444216 (Ally-2) (DCV/SOF+RBV 12-weeks)
Enrolled	% (n/N)	92% (11/12)	92% (22/24)
	95% CI	(61.5%, 99.8%)	(73.0%, 99.0%)
GT-1 Only	% (n/N)	91% (10/11)	91% (20/22)
	95% CI	(58.7%, 99.8%)	(70.8%, 98.9%)

Comparison: Ally-1: (DCV/SOF+ RBV 12 weeks in HCV)
Ally-2: (DCV/SOF 12 weeks in HCV/HIV co-infected)

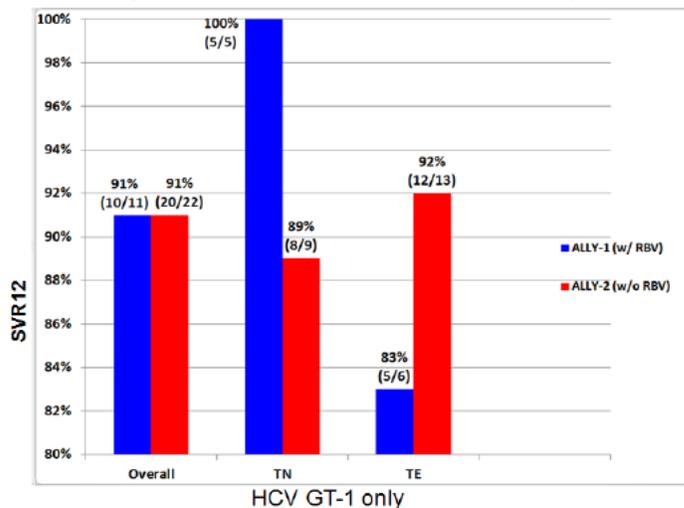


Figure 13: SVR12 for Subjects with CPT A at Baseline in Studies AI444215 and AI444216 by TN and TE (Treated Subjects)

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. In addition, there was only one study conducted in each subpopulation and thus, there is no replication of the findings.

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

4.1 Baseline Cirrhosis Status and Genotypes

❖ Study AI44215

It seems that the SVR12 rate of GT-1a (76.5%) in cirrhotic cohort was lower than that of GT-1b (100%) subjects. However, it is based on limited sample size and the associated uncertainties (Table 14). Given the sample sizes in the trial, subjects with CPT A and B at baseline had higher SVR12 rates than that of subjects with CPT C at baseline. The subgroup results for all subjects were listed in Table 26 in the Appendix.

Table 14: Subgroup Analysis of SVR12 of GT-1 Subjects Only for Study AI444215 by Baseline Cirrhosis Status and HCV Genotype (Treated Subjects)

Efficacy Parameter	Cirr	PostT	Total
Treated (ITT)			
N	37/ 45 (82.2)	39/ 41 (95.1)	76/ 86 (88.4)
HCV Genotype			
1A	26 / 34 (76.5)	30 / 31 (96.8)	56 / 65 (86.2)
1B	11 / 11 (100)	9 / 10 (90.0)	20 / 21 (95.2)
MELD Score Category at Baseline			
<15	27 / 31 (87.1)	. / . (.)	27 / 31 (87.1)
>=15	10 / 14 (71.4)	. / . (.)	10 / 14 (71.4)
Fibrosis Score Category -- 2			
F0 - F3	6 / 8 (75.0)	24 / 24 (100)	30 / 32 (93.8)
F4	31 / 37 (83.8)	15 / 16 (93.8)	46 / 53 (86.8)
missing	. / . (.)	. / 1 (0.00)	. / . (.)
Child-Pugh Score Category			
A	10 / 11 (90.9)	. / . (.)	10 / 11 (90.9)
B	22 / 24 (91.7)	. / . (.)	22 / 24 (91.7)
C	5 / 10 (50.0)	. / . (.)	5 / 10 (50.0)

❖ Study AI44216

Given the sample sizes in the trial, the SVR12 rates of GT-1a (96.2%) among TN and TE subjects combined was close to the GT-1b subjects (100%). Also, SVR12 rates were similar between cirrhotic and non-cirrhotic subjects at baseline (Table 15)

The subgroup results for all subjects were listed in Table 29 in Appendix.

Table 15: Subgroup Analysis of SVR12 of GT-1 Subjects Only for Study AI444216 by Baseline Cirrhosis Status and HCV Genotype (Treated Subjects)

Efficacy Parameter	TN	TE	Total
Treated (ITT)			
N	80 / 83 (96.4)	43 / 44 (97.7)	123 / 127 (96.9)
HCV Genotype			
1A	68 / 71 (95.8)	32 / 33 (97.0)	100 / 104 (96.2)
1B	12 / 12 (100)	11 / 11 (100)	23 / 23 (100)
Baseline Cirrhosis Category			
YES	8 / 9 (88.9)	12 / 13 (92.3)	20 / 22 (90.9)
NO	70 / 72 (97.2)	28 / 28 (100)	98 / 100 (98.0)
Inconclusive*	2 / 2 (100)	3 / 3 (100)	5 / 5 (100)

*: these 5 who had inconclusive were counted as no cirrhosis at baseline in the label.

4.2 Gender, Race, Age, and Geographic Region

Both studies enrolled all subjects in US. SVR12 rates in both studies were consistent across race and age group. In study AI444215, the SVR12 rate in males seems a slightly lower than that in females, while the SVR12 rate in females seems a slightly lower than that in males in study AI444216. Please see Table 25-29 in the Appendix for details.

4.3 Other Special/Subgroup Populations

The subgroup analysis for other baseline covariates were conducted on the all treated subject set, as well as GT-1 only for both studies. No other baseline factors, such as HCV RNA viral load at baseline, IL28B, or prior treatment, had a strong impact on the SVR12 rates. Please see Table 25-29 in the Appendix for details.

5. SUMMARY AND CONCLUSIONS

5.1 Statistical Issues and Collective Evidence

There were no major statistical issues. Two phase 3 studies were submitted to support the indication.

A total of 113 subjects, 60 subjects in the cirrhotic cohort and 53 subjects in the post-liver transplant cohort were enrolled into AI444215. In the cirrhotic cohort, the overall SVR12 rate was 83.3% (50/60, 95% CI: 71.5, 91.7), and the SVR12 rate in GT-1 infected subjects was 82.2% (37/45, 95% CI: 67.9, 92.0). The lower bound of the 95% CI, 67.9%, exceeded the 41.6% threshold. For the post-liver transplant cohort, the overall SVR12 rate was 94.3% (50/53, 95% CI: 84.3, 98.8) and the SVR12 rate in GT-1 infected subjects was 95.1% (39/41, 95% CI: 83.5, 99.4). The lower bound of the 95% CI, 83.5%, exceeded the 30% threshold. In the cirrhotic cohort, the SVR12 rates for GT-1 infected subjects were 90.9% (10/11, 95% CI: 58.6, 99.8) for those with Child-Pugh Score A (CPT A) at baseline, 91.7% (22/24, 95% CI: 73.0, 99.0) those with Child-Pugh Score B (CPT B) at baseline, and 50% (5/10, 95% CI: 18.7, 81.3) those with Child-Pugh Score C (CPT C) at baseline.

In conclusion, AI444215 demonstrated the efficacy of DCV/SOF/RBV for 12 weeks in HCV-1 infected subjects with compensated (CPT A) or decompensated (CPT B or CPT C) cirrhosis at baseline, and those with HCV recurrence after liver transplant. Chronic HCV-1 infected subjects with CPT C at baseline were limited in size and had a lower SVR12 rate compared to HCV genotype 1 subjects with CPT A or B. The optimal regimen for this subpopulation is uncertain.

In study AI444216, 101 TN HCV/HIV coinfecting subjects enrolled and received 12-weeks of DCV/SOF treatment and 52 TE HCV/HIV coinfecting subjects enrolled and received 12-weeks of DCV/SOF. For TN subjects who received 12-weeks of DCV/SOF, the overall SVR12 was 97.0% (98/101, 95% CI: 91.6, 99.4), and the SVR12 rate for GT-1 only was 96.4% (80/83, 95% CI: 89.8, 99.2). The lower bound of the 95% CI, 89.8%, was higher than the estimated historical rate of 29%. For TE subjects who received 12-week DCV/SOF, the overall SVR12 was 98.1% (51/52, 95% CI: 89.7, 100), and the SVR12 rate for GT-1 only was 97.7% (43/44, 95% CI: 88.0, 99.9). The lower bound of the 95% CI, 88.0%, was higher than the estimated historical rate of 5%. The SVR12 rates between TN and TE were comparable, and they are similar to the SVR12 rates of 12-weeks of Harvoni for HCV-1 mono-infected population in the Harvoni label.

For those who were TN HCV GT-1 coinfecting with HIV and treated with 12-weeks of DCV/SOF, the SVR12 rate was 89% (8/9, 95% CI: 51.8, 99.7) for subjects with cirrhosis at baseline, and the rate was 97% (72/74, 95% CI: 90.6, 99.7) for subjects without cirrhosis at baseline. For subjects who were TE HCV GT-1 co-infected with HIV and treated with 12-week of DCV/SOF, the SVR12 rate was 92% (12/13, 95% CI: 64.0, 99.8) for those with cirrhosis at baseline, and the rate was 100% (31/31, 95% CI: 88.8, 100) for those without cirrhosis at baseline.

The SVR rate was 90.9% (20/22, 95% CI: 70.8, 98.9) for HCV GT-1 HCV/HIV coinfecting TN and TE subjects with cirrhosis at baseline and treated with DCV/SOF for 12-weeks. The medical

reviewer classified these patients as having compensated cirrhosis. A similar rate was observed in AI444215 in HCV GT-1 infected subjects with CPT A at baseline (i.e. compensated cirrhosis) and treated with DCV/SOF/RBV for 12-weeks. The 95% CIs overlapped with no evidence that the addition of RBV improves response rates, although the data is limited. Therefore, it seems reasonable to treat HCV GT-1 subjects with CPT A at baseline with DCV/SOF 12-weeks without RBV.

In study AI444216, 10 subjects who had HCV GT-3 coinfecting with HIV were enrolled and treated with 12-week of DCV/SOF. The SVR12 rate for TN group was 100% (6/6) with 95% CI of [69%, 100%] and 100% (4/4) with 95% CI of [40%, 100%] in TE group

In conclusion, Study AI444216 demonstrated the efficacy of DCV/SOF 12-weeks in GT-1 HCV/HIV coinfecting subjects either TN or TE.

5.2 Conclusions and Recommendations

In conclusion, AI444215 and AI444216 demonstrated the efficacy of DCV/SOF with or without RBV for the treatment of chronic HCV infected, including those coinfecting with human immunodeficiency virus (HIV-1), those with compensated or decompensated cirrhosis, and those with HCV recurrence after liver transplant. Specifically, GT-1 CPT A subjects with or without cirrhosis should be treated with 12-weeks of DCV/SOF. GT-1 CPT B subjects with cirrhosis and post-liver transplant subjects should be treated with 12-weeks of DCV/SOF/RBV. Subjects with CPT C at baseline may have a reduced SVR12 rate if treated with 12-weeks of DCV/SOF/RBV.

Some additional information, which the reviewer did not evaluate, was also used to support the use of DCV/SOF/RBV 12-weeks to treat GT-3 with CPT A cirrhosis at baseline. Please see the clinical review for the details regarding this.

5.3 Labeling Recommendations

For AI444215 in Section 14 of the label, the efficacy table will only present the results for only GT-1 with CPT A, B, and C at baseline as follows:

ALLY-1: SVR12 in Genotype 1 Subjects with Child-Pugh A or B or C Cirrhosis or with HCV Genotype 1 Recurrence after Liver Transplantation Treated with DAKLINZA in Combination with Sofosbuvir and Ribavirin for 12 weeks		
Treatment Outcomes	Child-Pugh A or B or C, Cirrhosis n=45	Post-Liver Transplant n=41
SVR12		
Genotype 1	82% (37/45)	95% (39/41)
Child-Pugh A	91% (10/11)	-
Child-Pugh B	92% (22/24)	-
Child-Pugh C	50% (5/10)	
Genotype 1a	76% (26/34)	97% (30/31)
Genotype 1b	100% (11/11)	90% (9/10)

For AI444216 in the Section 14 of the label, those 5 subjects who had inconclusive cirrhosis status at baseline are included in the analysis as having no cirrhosis at baseline. Only GT-1 and GT-3 subjects' information were presented in the efficacy table as follows:

ALLY-2: SVR12 in Subjects with Genotype 1 and 3 HCV/HIV Coinfection Treated with DAKLINZA in Combination with Sofosbuvir for 12 Weeks	
Treatment Outcomes	Total n=137
SVR12	
Genotype 1	97% (123/127)
No cirrhosis ^a	98% (103/105)
With cirrhosis	91% (20/22)
Genotype 3 ^b	100% (10/10)
Outcomes for genotype 1 subjects without SVR12	
On-treatment virologic failure ^c	0.8% (1/127)
Relapse ^d	1.6% (2/126)
Missing post-treatment data	0.8% (1/126)

^a Includes 5 subjects with inconclusive cirrhosis status.

^b One subject with cirrhosis.

^c One subject had detectable HCV RNA at end of treatment.

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

APPENDICES

Table 16: Demographics and Baseline Characteristics for Study AI444215 (Treated Subjects)

Subgroup	Cirr	PostT	Total
Treated (ITT)			
N	60	53	113
Gender			
FEMALE	22 (36.7%)	15 (28.3%)	37 (32.7%)
MALE	38 (63.3%)	38 (71.7%)	76 (67.3%)
Race			
WHITE	57 (95.0%)	51 (96.2%)	108 (95.6%)
BLACK/AFRICAN AMERICAN	3 (5.0%)	1 (1.9%)	4 (3.5%)
KOREAN	. (. %)	1 (1.9%)	1 (0.9%)
Ethnicity			
HISPANIC/LATINO	25 (41.7%)	13 (24.5%)	38 (33.6%)
NOT HISPANIC/LATINO	35 (58.3%)	40 (75.5%)	75 (66.4%)
Age (Year)			
Mean (SE)	57.90 (1.220)	59.57 (1.133)	58.68 (0.838)
Median	58.00	59.00	59.00
Range	(19.00, 75.00)	(22.00, 82.00)	(19.00, 82.00)
STD	9.452	8.247	8.908
Age Category			
< 65	50 (83.3%)	42 (79.2%)	92 (81.4%)
>= 65	10 (16.7%)	11 (20.8%)	21 (18.6%)
Age Category 2 (Median)			
<59	31 (51.7%)	21 (39.6%)	52 (46.0%)
>=59	29 (48.3%)	32 (60.4%)	61 (54.0%)
Baseline HCV RNA log10 (IU/mL)			
Mean (SE)	6.01 (0.080)	6.61 (0.098)	6.29 (0.068)
Median	6.04	6.69	6.36
Range	(3.76, 7.36)	(4.31, 7.71)	(3.76, 7.71)
STD	0.617	0.711	0.724
Baseline HCV RNA Category (IU/mL)			
<800K	27 (45.0%)	6 (11.3%)	33 (29.2%)
>=800K	33 (55.0%)	47 (88.7%)	80 (70.8%)
Baseline HCV RNA Category 1 (IU/mL)			
<2,000K	37 (61.7%)	10 (18.9%)	47 (41.6%)
>=2,000K	23 (38.3%)	43 (81.1%)	66 (58.4%)
Baseline HCV RNA Category 2 (IU/mL)			
<6,000K	22 (36.7%)	6 (11.3%)	28 (24.8%)
>=6,000K	38 (63.3%)	47 (88.7%)	85 (75.2%)

Baseline HCV RNA Category 3 (IU/mL)			
<8000K	27 (45.0%)	6 (11.3%)	33 (29.2%)
>=8000K, <2,000K	10 (16.7%)	4 (7.5%)	14 (12.4%)
>=2,000K, <4,000K	14 (23.3%)	12 (22.6%)	26 (23.0%)
>=4,000K, <6,000K	4 (6.7%)	9 (17.0%)	13 (11.5%)
>=6,000K, <8,000K	2 (3.3%)	5 (9.4%)	7 (6.2%)
>=8,000K, <10,000K	. (. %)	5 (9.4%)	5 (4.4%)
>=10,000K, <12,000K	2 (3.3%)	. (. %)	2 (1.8%)
>=12,000K	1 (1.7%)	12 (22.6%)	13 (11.5%)
Baseline Genotype			
1A	34 (56.7%)	31 (58.5%)	65 (57.5%)
1B	11 (18.3%)	10 (18.9%)	21 (18.6%)
2	5 (8.3%)	. (. %)	5 (4.4%)
3	6 (10.0%)	11 (20.8%)	17 (15.0%)
4	4 (6.7%)	. (. %)	4 (3.5%)
6 C-L	. (. %)	1 (1.9%)	1 (0.9%)
Baseline BMI (kg/m^2)			
Mean (SE)	27.98 (0.538)	28.33 (0.554)	28.14 (0.385)
Median	27.85	27.90	27.90
Range	(19.20, 35.90)	(19.80, 35.10)	(19.20, 35.90)
STD	4.169	4.032	4.091
Baseline BMI Category (kg/m2)			
<=25	13 (21.7%)	8 (15.1%)	21 (18.6%)
25<=, <30	28 (46.7%)	27 (50.9%)	55 (48.7%)
>=30	19 (31.7%)	18 (34.0%)	37 (32.7%)
Baseline Cirrhosis Status			
Yes	59 (98.3%)		59 (98.3%)
Not Reported	1 (1.7%)		1 (1.7%)
MELD Score			
Mean (SE)	13.32 (0.560)		13.32 (0.560)
Median	13.00		13.00
Range	(8.00, 27.00)		(8.00, 27.00)
STD	4.339		4.339
MELD Category			
<15	39 (65.0%)		39 (65.0%)
>=15	21 (35.0%)		21 (35.0%)
Child-Pugh Score			
Mean (SE)	8.32 (0.267)		8.32 (0.267)
Median	8.00		8.00
Range	(5.00, 13.00)		(5.00, 13.00)
STD	2.071		2.071
Child-Pugh Category			
A	12 (20.0%)		12 (20.0%)
B	32 (53.3%)		32 (53.3%)
C	16 (26.7%)		16 (26.7%)
BSL Fibrosis Stage			
F0	. (. %)	6 (11.5%)	6 (5.4%)

F1	1 (1.7%)	10 (19.2%)	11 (9.8%)
F2	3 (5.0%)	7 (13.5%)	10 (8.9%)
F3	8 (13.3%)	13 (25.0%)	21 (18.8%)
F4	48 (80.0%)	16 (30.8%)	64 (57.1%)
IL28B genotype			
CC	13 (21.7%)	13 (24.5%)	26 (23.0%)
CT	33 (55.0%)	31 (58.5%)	64 (56.6%)
TT	14 (23.3%)	9 (17.0%)	23 (20.4%)
Prior Treatment (HCV)			
INTERFERON/RIBAVIRIN	32 (88.9%)	24 (77.4%)	56 (83.6%)
PEGIFN/RIBAVIRIN/BOC	2 (5.6%)	1 (3.2%)	3 (4.5%)
PEGIFN/RIBAVIRIN/TVR	1 (2.8%)	5 (16.1%)	6 (9.0%)
INTERFERON	1 (2.8%)	. (. %)	1 (1.5%)
OTHER	. (. %)	1 (3.2%)	1 (1.5%)
Prior Response Category			
NULL RESPONDER	10 (16.7%)	5 (9.4%)	15 (13.3%)
INDETERMINATE	9 (15.0%)	5 (9.4%)	14 (12.4%)
RELAPSER	7 (11.7%)	10 (18.9%)	17 (15.0%)
INTOLERANCE	7 (11.7%)	4 (7.5%)	11 (9.7%)
PARTIAL RESPONDER	2 (3.3%)	2 (3.8%)	4 (3.5%)
BREAKTHROUGH	. (. %)	3 (5.7%)	3 (2.7%)
HCV RNA NEVER UNDETECTABLE ON TREATMENT	1 (1.7%)	2 (3.8%)	3 (2.7%)
MISSING	24 (40.0%)	22 (41.5%)	46 (40.7%)
Country			
USA	60 (100.0%)	53 (100.0%)	113 (100.0%)
Region			
NORTH AMERICA	60 (100.0%)	53 (100.0%)	113 (100.0%)

Table 17: Demographics and Baseline Characteristics of GT-1 Subject Only for Study AI444215 (treated Subjects)

Subgroup	Cirr	PostT	Total
Treated (ITT)			
N	45	41	86
Gender			
FEMALE	20 (44.4%)	13 (31.7%)	33 (38.4%)
MALE	25 (55.6%)	28 (68.3%)	53 (61.6%)
Race			
WHITE	43 (95.6%)	39 (95.1%)	82 (95.3%)
BLACK/AFRICAN AMERICAN	2 (4.4%)	1 (2.4%)	3 (3.5%)
KOREAN	. (. %)	1 (2.4%)	1 (1.2%)
Ethnicity			
HISPANIC/LATINO	20 (44.4%)	10 (24.4%)	30 (34.9%)
NOT HISPANIC/LATINO	25 (55.6%)	31 (75.6%)	56 (65.1%)

Age (Year)			
Mean (SE)	57.87 (1.481)	59.63 (1.442)	58.71 (1.035)
Median	59.00	60.00	59.50
Range	(19.00, 75.00)	(22.00, 82.00)	(19.00, 82.00)
STD	9.938	9.235	9.594
Age Category			
< 65	37 (82.2%)	31 (75.6%)	68 (79.1%)
>= 65	8 (17.8%)	10 (24.4%)	18 (20.9%)
Age Category 2 (Median)			
<59	20 (44.4%)	16 (39.0%)	36 (41.9%)
>=59	25 (55.6%)	25 (61.0%)	50 (58.1%)
Baseline HCV RNA log10 (IU/mL)			
Mean (SE)	6.08 (0.090)	6.64 (0.104)	6.35 (0.074)
Median	6.06	6.72	6.42
Range	(3.76, 7.36)	(4.31, 7.71)	(3.76, 7.71)
STD	0.604	0.666	0.689
Baseline HCV RNA Category (IU/mL)			
<800K	19 (42.2%)	4 (9.8%)	23 (26.7%)
>=800K	26 (57.8%)	37 (90.2%)	63 (73.3%)
Baseline HCV RNA Category 1 (IU/mL)			
<2,000K	25 (55.6%)	7 (17.1%)	32 (37.2%)
>=2,000K	20 (44.4%)	34 (82.9%)	54 (62.8%)
Baseline HCV RNA Category 2 (IU/mL)			
<6,000K	17 (37.8%)	4 (9.8%)	21 (24.4%)
>=6,000K	28 (62.2%)	37 (90.2%)	65 (75.6%)
Baseline HCV RNA Category 3 (IU/mL)			
<8000K	19 (42.2%)	4 (9.8%)	23 (26.7%)
>=8000K, <2,000K	6 (13.3%)	3 (7.3%)	9 (10.5%)
>=2,000K, <4,000K	11 (24.4%)	9 (22.0%)	20 (23.3%)
>=4,000K, <6,000K	4 (8.9%)	6 (14.6%)	10 (11.6%)
>=6,000K, <8,000K	2 (4.4%)	5 (12.2%)	7 (8.1%)
>=8,000K, <10,000K	. (. %)	5 (12.2%)	5 (5.8%)
>=10,000K, <12,000K	2 (4.4%)	. (. %)	2 (2.3%)
>=12,000K	1 (2.2%)	9 (22.0%)	10 (11.6%)
Baseline Genotype			
1A	34 (75.6%)	31 (75.6%)	65 (75.6%)
1B	11 (24.4%)	10 (24.4%)	21 (24.4%)
Baseline BMI (kg/m^2)			
Mean (SE)	27.66 (0.669)	28.29 (0.645)	27.96 (0.465)
Median	27.80	27.80	27.80
Range	(19.20, 35.90)	(19.80, 35.10)	(19.20, 35.90)
STD	4.491	4.129	4.309
Baseline BMI Category (kg/m2)			
<=25	13 (28.9%)	6 (14.6%)	19 (22.1%)

25<=, <30	17 (37.8%)	22 (53.7%)	39 (45.3%)
>=30	15 (33.3%)	13 (31.7%)	28 (32.6%)
Baseline Cirrhosis Status			
Yes	45 (100%)		45 (100%)
MELD Score			
Mean (SE)	12.69 (0.505)		12.69 (0.505)
Median	12.00		12.00
Range	(8.00, 20.00)		(8.00, 20.00)
STD	3.390		3.390
MELD Category			
<15	31 (68.9%)		31 (68.9%)
>=15	14 (31.1%)		14 (31.1%)
Child-Pugh Score			
Mean (SE)	8.02 (0.301)		8.02 (0.301)
Median	8.00		8.00
Range	(5.00, 13.00)		(5.00, 13.00)
STD	2.017		2.017
Child-Pugh Category			
A	11 (24.4%)		11 (24.4%)
B	24 (53.3%)		24 (53.3%)
C	10 (22.2%)		10 (22.2%)
BSL Fibrosis Stage			
F0	. (. %)	4 (10.0%)	4 (4.7%)
F1	1 (2.2%)	7 (17.5%)	8 (9.4%)
F2	2 (4.4%)	6 (15.0%)	8 (9.4%)
F3	5 (11.1%)	7 (17.5%)	12 (14.1%)
F4	37 (82.2%)	16 (40.0%)	53 (62.4%)
IL28B genotype			
CC	7 (15.6%)	9 (22.0%)	16 (18.6%)
CT	26 (57.8%)	24 (58.5%)	50 (58.1%)
TT	12 (26.7%)	8 (19.5%)	20 (23.3%)
Prior Treatment (HCV)			
INTERFERON/RIBAVIRIN	24 (88.9%)	19 (76.0%)	43 (82.7%)
PEGIFN/RIBAVIRIN/BOC	2 (7.4%)	1 (4.0%)	3 (5.8%)
PEGIFN/RIBAVIRIN/TVR	1 (3.7%)	4 (16.0%)	5 (9.6%)
OTHER	. (. %)	1 (4.0%)	1 (1.9%)
Prior Response Category			
NULL RESPONDER	8 (17.8%)	5 (12.2%)	13 (15.1%)
INDETERMINATE	8 (17.8%)	5 (12.2%)	13 (15.1%)
RELAPSER	6 (13.3%)	6 (14.6%)	12 (14.0%)
INTOLERANCE	4 (8.9%)	3 (7.3%)	7 (8.1%)
BREAKTHROUGH	. (. %)	3 (7.3%)	3 (3.5%)
PARTIAL RESPONDER	1 (2.2%)	1 (2.4%)	2 (2.3%)
HCV RNA NEVER UND ECTABLE ON TREATMENT	. (. %)	2 (4.9%)	2 (2.3%)
MISSING	18 (40.0%)	16 (39.0%)	34 (39.5%)

Country			
USA	45 (100.0%)	41 (100.0%)	86 (100.0%)
Region			
NORTH AMERICA	45 (100.0%)	41 (100.0%)	86 (100.0%)

Table 18: Demographics and Baseline Characteristics for Study AI444216 (Treated Subjects)

Subgroup	TN	TE	Total
Treated (ITT)			
N	101	52	153
Gender			
FEMALE	9 (8.9%)	9 (17.3%)	18 (11.8%)
MALE	92 (91.1%)	43 (82.7%)	135 (88.2%)
Race			
WHITE	66 (65.3%)	31 (59.6%)	97 (63.4%)
BLACK/AFRICAN AMERICAN	30 (29.7%)	20 (38.5%)	50 (32.7%)
AMERICAN INDIAN/ALASKA NATIVE	2 (2.0%)	1 (1.9%)	3 (2.0%)
ASIAN OTHER	1 (1.0%)	. (. %)	1 (0.7%)
OTHER	2 (2.0%)	. (. %)	2 (1.3%)
Race Category			
WHITE	66 (65.3%)	31 (59.6%)	97 (63.4%)
BLACK/AFRICAN AMERICAN	30 (29.7%)	20 (38.5%)	50 (32.7%)
AMERICAN INDIAN/ALASKA NATIVE	2 (2.0%)	1 (1.9%)	3 (2.0%)
ASIAN OTHER	1 (1.0%)	. (. %)	1 (0.7%)
OTHER: MOORISH-AMERICAN	1 (1.0%)	. (. %)	1 (0.7%)
OTHER: PUERTO RICAN	1 (1.0%)	. (. %)	1 (0.7%)
Ethnicity			
HISPANIC/LATINO	18 (17.8%)	10 (19.2%)	28 (18.3%)
NOT HISPANIC/LATINO	83 (82.2%)	42 (80.8%)	125 (81.7%)
Age (Year)			
Mean (SE)	50.12 (0.972)	55.71 (0.862)	52.02 (0.736)
Median	52.00	56.50	53.00
Range	(24.00, 71.00)	(43.00, 66.00)	(24.00, 71.00)
std	9.770	6.213	9.100
Age Category			
< 65	96 (95.0%)	49 (94.2%)	145 (94.8%)
>= 65	5 (5.0%)	3 (5.8%)	8 (5.2%)
Age Category 2			
<65	96 (95.0%)	49 (94.2%)	145 (94.8%)
>=65, <75	5 (5.0%)	3 (5.8%)	8 (5.2%)

Baseline HCV RNA log10 (IU/mL)			
Mean (SE)	6.50 (0.075)	6.52 (0.109)	6.51 (0.062)
Median	6.74	6.68	6.71
Range	(3.32, 7.61)	(3.87, 7.88)	(3.32, 7.88)
std	0.758	0.789	0.766
Baseline HCV RNA Category (IU/mL)			
<800K	22 (21.8%)	8 (15.4%)	30 (19.6%)
>=800K	79 (78.2%)	44 (84.6%)	123 (80.4%)
Baseline HCV RNA Category 1 (IU/mL)			
<2,000K	35 (34.7%)	17 (32.7%)	52 (34.0%)
>=2,000K	66 (65.3%)	35 (67.3%)	101 (66.0%)
Baseline HCV RNA Category 2 (IU/mL)			
<6,000K	58 (57.4%)	33 (63.5%)	91 (59.5%)
>=6,000K	43 (42.6%)	19 (36.5%)	62 (40.5%)
Baseline HCV RNA Category 3 (IU/mL)			
<8000K	22 (21.8%)	8 (15.4%)	30 (19.6%)
>=800K, <2,000K	13 (12.9%)	9 (17.3%)	22 (14.4%)
>=2,000K, <4,000K	10 (9.9%)	7 (13.5%)	17 (11.1%)
>=4,000K, <6,000K	13 (12.9%)	9 (17.3%)	22 (14.4%)
>=6,000K, <8,000K	8 (7.9%)	3 (5.8%)	11 (7.2%)
>=8,000K, <10,000K	5 (5.0%)	3 (5.8%)	8 (5.2%)
>=10,000K, <12,000K	8 (7.9%)	2 (3.8%)	10 (6.5%)
>=12,000K	22 (21.8%)	11 (21.2%)	33 (21.6%)
Baseline Genotype			
1A	71 (70.3%)	33 (63.5%)	104 (68.0%)
1B	12 (11.9%)	11 (21.2%)	23 (15.0%)
2	11 (10.9%)	2 (3.8%)	13 (8.5%)
3	6 (5.9%)	4 (7.7%)	10 (6.5%)
4	1 (1.0%)	2 (3.8%)	3 (2.0%)
Baseline BMI (kg/m^2)			
Mean (SE)	25.91 (0.352)	27.04 (0.556)	26.30 (0.302)
Median	25.10	27.25	26.00
Range	(18.10, 34.70)	(19.00, 35.00)	(18.10, 35.00)
std	3.542	4.010	3.734
Baseline BMI Category (kg/m2)			
<=25	50 (49.5%)	17 (32.7%)	67 (43.8%)
25<=, <30	37 (36.6%)	22 (42.3%)	59 (38.6%)
>=30	14 (13.9%)	13 (25.0%)	27 (17.6%)
Baseline Cirrhosis Status			
YES	9 (8.9%)	15 (28.8%)	24 (15.7%)
NO	90 (89.1%)	34 (65.4%)	124 (81.0%)
.	2 (2.0%)	3 (5.8%)	5 (3.3%)
Baseline Fibrosis Stage			
F0	24 (24.5%)	8 (15.4%)	32 (21.3%)
F1	23 (23.5%)	9 (17.3%)	32 (21.3%)

F2	10 (10.2%)	7 (13.5%)	17 (11.3%)
F3	19 (19.4%)	10 (19.2%)	29 (19.3%)
F4	22 (22.4%)	18 (34.6%)	40 (26.7%)
IL28B genotype			
CC	28 (27.7%)	13 (25.0%)	41 (26.8%)
CT	48 (47.5%)	30 (57.7%)	78 (51.0%)
TT	25 (24.8%)	9 (17.3%)	34 (22.2%)
Baseline HIV RNA VL (copies/mL)			
Mean (SE)	40.99 (0.977)	40.29 (0.930)	40.75 (0.717)
Median	39.00	39.00	39.00
Range	(39.00, 126.0)	(39.00, 83.00)	(39.00, 126.0)
std	9.818	6.708	8.867
Baseline HIV RNA VL Category (<500 copies/mL)			
<500K	101 (100.0%)	52 (100.0%)	153 (100.0%)
CD4 Count			
Mean (SE)	549.1 (21.58)	687.6 (38.84)	595.6 (20.02)
Median	520.0	636.0	560.5
Range	(122.0, 1147)	(262.0, 1470)	(122.0, 1470)
std	216.8	277.4	246.8
CD4 Category - 1			
<200	4 (4.0%)	. (. %)	4 (2.6%)
>=200	97 (96.0%)	51 (100.0%)	148 (97.4%)
CD4 Category - 2			
200 - < 500	42 (41.6%)	12 (23.5%)	54 (35.5%)
< 200	4 (4.0%)	. (. %)	4 (2.6%)
>= 500	55 (54.5%)	39 (76.5%)	94 (61.8%)
CD8 Count			
Mean (SE)	813.7 (48.73)	741.1 (48.23)	789.4 (36.21)
Median	683.0	648.0	663.5
Range	(118.0, 3481)	(220.0, 1630)	(118.0, 3481)
std	489.7	344.5	446.4
Country			
USA	101 (100.0%)	52 (100.0%)	153 (100.0%)
Region			
NORTH AMERICA	101 (100.0%)	52 (100.0%)	153 (100.0%)
DCV Dose Category			
30 MG	47 (46.5%)	23 (44.2%)	70 (45.8%)
60 MG	31 (30.7%)	18 (34.6%)	49 (32.0%)
90 MG	23 (22.8%)	11 (21.2%)	34 (22.2%)
Prior Treatment (HCV)			
INTERFERON/RIBAVIRIN	1 (100.0%)	37 (71.2%)	38 (71.7%)
PEGIFN/RIBAVIRIN/BOC	. (. %)	5 (9.6%)	5 (9.4%)
PEGIFN/RIBAVIRIN/TRV	. (. %)	5 (9.6%)	5 (9.4%)

SOFOSBUVIR/RIBAVIRIN	. (. %)	3 (5.8%)	3 (5.7%)
INTERFERON	. (. %)	1 (1.9%)	1 (1.9%)
OTHER	. (. %)	1 (1.9%)	1 (1.9%)
Prior Response Category			
NULL RESPONDER	1 (1.0%)	17 (32.7%)	18 (11.8%)
RELAPSER	. (. %)	14 (26.9%)	14 (9.2%)
INTOLERANCE	. (. %)	8 (15.4%)	8 (5.2%)
PARTIAL RESPONDER	. (. %)	7 (13.5%)	7 (4.6%)
INDETERMINATE	. (. %)	3 (5.8%)	3 (2.0%)
BREAKTHROUGH	. (. %)	2 (3.8%)	2 (1.3%)
HCV RNA NEVER UNDETECTABLE ON TREATMENT	. (. %)	1 (1.9%)	1 (0.7%)
cART Regimen			
PI	47 (46.5%)	23 (44.2%)	70 (45.8%)
NNRTI	28 (27.7%)	12 (23.1%)	40 (26.1%)
NONE	1 (1.0%)	1 (1.9%)	2 (1.3%)
OTHER	25 (24.8%)	16 (30.8%)	41 (26.8%)
cART Individual			
ATAZANAVIR	19 (25.3%)	12 (34.3%)	31 (28.2%)
DARUNAVIR	19 (25.3%)	11 (31.4%)	30 (27.3%)
EFAVIRENZ	18 (24.0%)	8 (22.9%)	26 (23.6%)
LOPINA VIR	9 (12.0%)	. (. %)	9 (8.2%)
NEVIRAPINE	5 (6.7%)	3 (8.6%)	8 (7.3%)
RILPIVIRINE	5 (6.7%)	1 (2.9%)	6 (5.5%)

Table 19: Demographics and Baseline Characteristics of TN8 Arm only for Study AI444216 (Treated Subjects)

Subgroup	TN8

Treated (ITT)	
N	50
Gender	
FEMALE	8 (16.0%)
MALE	42 (84.0%)
Race	
ASIAN OTHER	1 (2.0%)
BLACK/AFRICAN AMERICAN	19 (38.0%)
NATIVE HAWAIIAN/OTHER PACIF	2 (4.0%)
WHITE	28 (56.0%)
Race Category	
ASIAN OTHER	1 (2.0%)
BLACK/AFRICAN AMERICAN	19 (38.0%)
NATIVE HAWAIIAN/OTHER PACIF	2 (4.0%)
WHITE	28 (56.0%)

Age (Year)		
MSE	50.80	(1.300)
median		50.50
Range	(28.00,	75.00)
std		9.194
Age Category		
< 65	47	(94.0%)
>= 65	3	(6.0%)
Age Category 2		
<65	47	(94.0%)
>=65, <75	1	(2.0%)
>=75	2	(4.0%)
Baseline HCV RNA log10 (IU/mL)		
MSE	6.40	(0.100)
median		6.44
Range	(4.19,	7.48)
std		0.710
Baseline HCV RNA Category (IU/mL)		
<800K	6	(12.0%)
>=800K	44	(88.0%)
Baseline HCV RNA Category 1 (IU/mL)		
<2,000K	18	(36.0%)
>=2,000K	32	(64.0%)
Baseline HCV RNA Category 2 (IU/mL)		
<6,000K	34	(68.0%)
>=6,000K	16	(32.0%)
Baseline BMI (kg/m^2)		
MSE	24.77	(0.534)
median		24.55
Range	(16.60,	34.40)
std		3.773
Baseline BMI Category (kg/m2)		
25<=, <30	15	(30.0%)
<=25	28	(56.0%)
>=30	7	(14.0%)
Baseline Cirrhosis Status		
.	1	(2.0%)
NO	44	(88.0%)
YES	5	(10.0%)
Baseline HIV RNA VL (copies/mL)		
MSE	69.00	(27.00)
median		39.00
Range	(39.00,	1390)
std		190.9
Baseline HIV RNA VL Category (<500 copies/mL)		

<500K	49 (98.0%)
>=500K	1 (2.0%)
IL28B genotype	
CC	13 (26.0%)
CT	28 (56.0%)
TT	9 (18.0%)
cART Regimen	
NNRTI	10 (20.0%)
NONE	2 (4.0%)
OTHER	9 (18.0%)
PI	29 (58.0%)
cART Individual	
ATAZANAVIR	5 (12.8%)
DARUNAVIR	21 (53.8%)
EFAVIRENZ	8 (20.5%)
LOPINAVIR	3 (7.7%)
NEVIRAPINE	1 (2.6%)
RILPIVIRINE	1 (2.6%)
Ethnicity	
HISPANIC/LATINO	8 (16.0%)
NOT HISPANIC/LATINO	42 (84.0%)
Sub-Cohort Classification	
F0	16 (32.0%)
F1	9 (18.0%)
F2	2 (4.0%)
F3	8 (16.0%)
F4	15 (30.0%)
Region	
NORTH AMERICA	50 (100.0%)
CD8 Count	
MSE	847.8 (55.73)
median	821.0
Range	(212.0, 1849)
std	394.1
CD4 Count	
MSE	587.9 (39.90)
median	575.0
Range	(157.0, 1430)
std	282.2
CD4 Category - 1	
<200	1 (2.0%)
>=200	49 (98.0%)
CD4 Category - 2	
200 - < 500	21 (42.0%)
< 200	1 (2.0%)
>= 500	28 (56.0%)

DCV Dose Category	
30 MG	29 (58.0%)
60 MG	12 (24.0%)
90 MG	9 (18.0%)

Table 20: Secondary Efficacy Results of GT-1 Subjects Only for Study AI444215 (Treated Subjects)

Treated Subjects Parameters analyzed	Cirr (N=45)	PostT (N=41)	Total (N=86)
SVR12	37/45 (82.2%) (68.0%, 92.0%)	39/41 (95.1%) (83.5%, 99.4%)	76/86 (88.4%) (79.7%, 94.3%)
EOT	44/45 (97.8%) (88.2%, 99.9%)	41/41 (100%) (91.4%, 100%)	85/86 (98.8%) (93.7%, 100%)
Relapse rate	7/44 (15.9%)	2/41 (4.9%)	
RVR at WK 4	24/44 (54.6%) (38.9%, 69.6%)	25/41 (61.0%) (44.5%, 75.8%)	49/85 (57.7%) (46.5%, 68.3%)
cEVR at WK 12	42/43 (97.7%) (87.7%, 99.9%)	41/41 (100%) (91.4%, 100%)	83/84 (98.8%) (93.5%, 100%)
eRVR at WK 4 & 12	23/45 (51.1%) (35.8%, 66.3%)	25/41 (61.0%) (44.5%, 75.8%)	48/86 (55.8%) (44.7%, 66.5%)

Table 21: Secondary Efficacy Results of All Subjects for Study AI444215 (Treated Subjects)

Treated Subjects Parameters analyzed	Cirr (N=60)	PostT (N=53)	Total (N=113)
SVR12	50/60 (83.3%) (71.5%, 91.7%)	50/53 (94.3%) (84.3%, 98.8%)	100/113 (88.5%) (81.1%, 93.7%)
EOT	58/60 (96.7%) (88.5%, 99.6%)	53/53 (100%) (93.3%, 100%)	111/113 (98.2%) (93.8%, 99.8%)
Relapse rate	9/58 (15.5%)	3/53 (5.7%)	
RVR at WK 4	32/59 (54.2%) (40.8%, 67.3%)	30/53 (56.6%) (42.3%, 70.2%)	62/112 (55.4%) (45.7%, 64.8%)
cEVR at WK 12	56/58 (96.6%) (88.1%, 99.6%)	52/53 (98.1%) (89.9%, 100%)	108/111 (97.3%) (92.3%, 99.4%)
eRVR at WK 4 & 12	31/60 (51.7%) (38.4%, 64.8%)	29/53 (54.7%) (40.5%, 68.4%)	60/113 (53.1%) (43.5%, 62.6%)

Table 22: Secondary Efficacy Results of GT-1 Subjects Only for Study AI444216 (Treated Subjects)

Treated Subjects Parameters analyzed	Treatment-Naïve 12 weeks (N=83)	Treatment-Experienced 12 weeks (N=44)	Total (N=127)
SVR12	96.4% (80/83) (89.8%, 99.3%)	97.7% (43/44) (88.0%, 100%)	96.9% (123/127) (92.1%, 99.1%)
EOT	98.8% (82/83) (93.5%, 100%)	100% (44/44) (92.0%, 100%)	99.2% (126/127) (95.7%, 100%)
Relapse rate	2.4% (2/82)	2.3% (1/44)	
RVR at WK 4	69.9% (58/83) (58.8%, 79.5%)	65.9% (29/44) (50.1%, 79.5%)	68.5% (87/127) (59.7%, 76.5%)
cEVR at WK 12	96.4% (80/83) (89.8%, 99.3%)	97.7% (43/44) (88.0%, 100%)	96.9% (123/127) (92.1%, 99.1%)
eRVR at WK 4 & 12	68.7% (57/83) (57.6%, 78.4%)	65.9% (29/44) (50.1%, 79.5%)	67.7% (86/127) (58.9%, 75.7%)

Table 23: Secondary Efficacy Results of GT-1 and GT-3 Subjects Only for Study AI444216 (Treated Subjects)

Treated Subjects Parameters analyzed	Treatment-Naïve 12 weeks (N=89)	Treatment-Experienced 12 weeks (N=48)	Total (N=137)
SVR12	96.6% (86/89) (90.5%, 99.3%)	97.9% (47/48) (88.9%, 100%)	97.1% (133/137) (92.7%, 99.2%)
EOT	98.9% (88/89) (93.9%, 100%)	100% (48/48) (92.6%, 100%)	99.3% (136/137) (96.0%, 100%)
Relapse rate	2.3% (2/88)	2.1% (1/48)	
RVR at WK 4	70.8% (63/89) (60.2%, 80.0%)	64.6% (31/48) (49.5%, 77.8%)	68.6% (94/137) (60.1%, 76.3%)
cEVR at WK 12	96.6% (86/89) (90.5%, 99.3%)	97.9% (47/48) (88.9%, 100%)	97.1% (133/137) (92.7%, 99.2%)
eRVR at WK 4 & 12	69.7% (62/89) (59.0%, 79.0%)	64.6% (31/48) (49.6%, 77.8%)	67.9% (93/137) (59.4%, 75.6%)

Table 24: Secondary Efficacy Results of All Subjects for Study AI444216 (Treated Subjects)

Treated Subjects Parameters analyzed	Treatment-Naïve 12 weeks (N=101)	Treatment-Experienced 12 weeks (N=52)	Treatment-Naïve 8 weeks (N=50)
SVR12	97.0% (98/101) (91.6%, 99.4%)	98.1% (51/52) (89.7%, 100%)	76.0% (38/50) (61.8%, 86.9%)
EOT	99.0% (100/101) (94.6%, 100%)	100% (52/52) (93.2%, 100%)	100% (50/50) (92.9%, 100%)
Relapse rate	2% (2/100)*	1.9% (1/52)	24.0% (12/50)
RVR at WK 4	70.3% (71/101) (60.4%, 79.0%)	63.5% (33/52) (49.0%, 76.4%)	78.0% (39/50) (64.0%, 88.5%)
cEVR at WK 12	96.0% (97/101) (90.2%, 98.9%)	98.1% (51/52) (89.7%, 100%)	
eRVR at WK 4 & 12	68.3% (69/101) (58.3%, 77.2%)	63.5% (33/52) (49.0%, 76.4%)	

Table 25: Subgroup Analyses of SVR12 of GT-1 Subjects Only for Study AI444215 (Treated Subjects)

Efficacy Parameter	Cirr	PostT	Total
Treated (ITT)			
N	37/ 45 (82.2)	39/ 41 (95.1)	76/ 86 (88.4)
Gender			
FEMALE	18 / 20 (90.0)	13 / 13 (100)	31 / 33 (93.9)
MALE	19 / 25 (76.0)	26 / 28 (92.9)	45 / 53 (84.9)
Race			
BLACK/AFRICAN A	2 / 2 (100)	1 / 1 (100)	3 / 3 (100)
KOREAN	. / . (.)	1 / 1 (100)	1 / 1 (100)
WHITE	35 / 43 (81.4)	37 / 39 (94.9)	72 / 82 (87.8)
Ethnicity			
HISPANIC/LATINO	15 / 20 (75.0)	8 / 10 (80.0)	23 / 30 (76.7)
NOT HISPANIC/LA	22 / 25 (88.0)	31 / 31 (100)	53 / 56 (94.6)
Age Group 1			
< 65	29 / 37 (78.4)	30 / 31 (96.8)	59 / 68 (86.8)
>= 65	8 / 8 (100)	9 / 10 (90.0)	17 / 18 (94.4)
Age Group 2			
<59	15 / 20 (75.0)	16 / 16 (100)	31 / 36 (86.1)
>=59	22 / 25 (88.0)	23 / 25 (92.0)	45 / 50 (90.0)
HCV RNA BSL <800K			
<800K	16 / 19 (84.2)	4 / 4 (100)	20 / 23 (87.0)
>=800K	21 / 26 (80.8)	35 / 37 (94.6)	56 / 63 (88.9)
HCV RNA BSL <2,000K			
<2,000K	21 / 25 (84.0)	7 / 7 (100)	28 / 32 (87.5)
>=2,000K	16 / 20 (80.0)	32 / 34 (94.1)	48 / 54 (88.9)
HCV RNA BSL <6,000K			
<6,000K	15 / 17 (88.2)	4 / 4 (100)	19 / 21 (90.5)
>=6,000K	22 / 28 (78.6)	35 / 37 (94.6)	57 / 65 (87.7)
HCV RNA BSL Categories			
<8000K	16 / 19 (84.2)	4 / 4 (100)	20 / 23 (87.0)
>=10,000K, <12,	. / 2 (0.00)	. / . (.)	. / . (.)
>=12,000K	1 / 1 (100)	9 / 9 (100)	10 / 10 (100)
>=2,000K, <4,00	9 / 11 (81.8)	8 / 9 (88.9)	17 / 20 (85.0)
>=4,000K, <6,00	4 / 4 (100)	6 / 6 (100)	10 / 10 (100)
>=6,000K, <8,00	2 / 2 (100)	4 / 5 (80.0)	6 / 7 (85.7)
>=8,000K, <10,0	. / . (.)	5 / 5 (100)	5 / 5 (100)
>=800K, <2,000K	5 / 6 (83.3)	3 / 3 (100)	8 / 9 (88.9)
HCV Genotype			
1A	26 / 34 (76.5)	30 / 31 (96.8)	56 / 65 (86.2)
1B	11 / 11 (100)	9 / 10 (90.0)	20 / 21 (95.2)

BMI category				
25<=, <30	12 / 17 (70.6)	21 / 22 (95.5)	33 / 39 (84.6)	
<=25	13 / 13 (100)	6 / 6 (100)	19 / 19 (100)	
>=30	12 / 15 (80.0)	12 / 13 (92.3)	24 / 28 (85.7)	
MELD Score Category at Baseline				
<15	27 / 31 (87.1)	. / . (.)	27 / 31 (87.1)	
>=15	10 / 14 (71.4)	. / . (.)	10 / 14 (71.4)	
IL28B Genotype				
CC	7 / 7 (100)	9 / 9 (100)	16 / 16 (100)	
CT	22 / 26 (84.6)	22 / 24 (91.7)	44 / 50 (88.0)	
TT	8 / 12 (66.7)	8 / 8 (100)	16 / 20 (80.0)	
Fibrosis Score Category				
F0	. / . (.)	4 / 4 (100)	4 / 4 (100)	
F1	1 / 1 (100)	7 / 7 (100)	8 / 8 (100)	
F2	1 / 2 (50.0)	6 / 6 (100)	7 / 8 (87.5)	
F3	4 / 5 (80.0)	7 / 7 (100)	11 / 12 (91.7)	
F4	31 / 37 (83.8)	15 / 16 (93.8)	46 / 53 (86.8)	
Fibrosis Score Category -- 1				
F0 - F2	2 / 3 (66.7)	17 / 17 (100)	19 / 20 (95.0)	
F3 - F4	35 / 42 (83.3)	22 / 23 (95.7)	57 / 65 (87.7)	
missing	. / . (.)	. / 1 (0.00)	. / . (.)	
Fibrosis Score Category -- 2				
F0 - F3	6 / 8 (75.0)	24 / 24 (100)	30 / 32 (93.8)	
F4	31 / 37 (83.8)	15 / 16 (93.8)	46 / 53 (86.8)	
missing	. / . (.)	. / 1 (0.00)	. / . (.)	
Child-Pugh Score Category				
A	10 / 11 (90.9)	. / . (.)	10 / 11 (90.9)	
B	22 / 24 (91.7)	. / . (.)	22 / 24 (91.7)	
C	5 / 10 (50.0)	. / . (.)	5 / 10 (50.0)	
Prior Treatment				
INTERFERON/RIBA	19 / 24 (79.2)	18 / 19 (94.7)	37 / 43 (86.0)	
OTHER	. / . (.)	1 / 1 (100)	1 / 1 (100)	
PEGIFN/RIBAVIRI	1 / 2 (50.0)	1 / 1 (100)	2 / 3 (66.7)	
PEGIFN/RIBAVIRI	1 / 1 (100)	4 / 4 (100)	5 / 5 (100)	
Prior Response Category				
BREAKTHROUGH	16 / 18 (88.9)	15 / 16 (93.8)	31 / 34 (91.2)	
HCV RNA NEVER U	. / . (.)	3 / 3 (100)	3 / 3 (100)	
INDETERMINATE	. / . (.)	2 / 2 (100)	2 / 2 (100)	
INDETERMINATE	6 / 8 (75.0)	5 / 5 (100)	11 / 13 (84.6)	
INTOLERANCE	2 / 4 (50.0)	2 / 3 (66.7)	4 / 7 (57.1)	
NULL RESPONDER	6 / 8 (75.0)	5 / 5 (100)	11 / 13 (84.6)	
PARTIAL RESPOND	1 / 1 (100)	1 / 1 (100)	2 / 2 (100)	
RELAPSER	6 / 6 (100)	6 / 6 (100)	12 / 12 (100)	
Country				
USA	37 / 45 (82.2)	39 / 41 (95.1)	76 / 86 (88.4)	

Table 26: Subgroup Analyses of SVR12 All Subjects for Study AI444215 (Treated Subjects)

Efficacy Parameter	Cirr	PostT	Total
Treated (ITT)			
N	50/ 60 (83.3)	50/ 53 (94.3)	100/113 (88.5)
Gender			
FEMALE	20 / 22 (90.9)	15 / 15 (100)	35 / 37 (94.6)
MALE	30 / 38 (78.9)	35 / 38 (92.1)	65 / 76 (85.5)
Race			
BLACK/AFRICAN A	3 / 3 (100)	1 / 1 (100)	4 / 4 (100)
KOREAN	. / . (.)	1 / 1 (100)	1 / 1 (100)
WHITE	47 / 57 (82.5)	48 / 51 (94.1)	95 /108 (88.0)
Ethnicity			
HISPANIC/LATINO	19 / 25 (76.0)	11 / 13 (84.6)	30 / 38 (78.9)
NOT HISPANIC/LA	31 / 35 (88.6)	39 / 40 (97.5)	70 / 75 (93.3)
Age Group 1			
< 65	40 / 50 (80.0)	40 / 42 (95.2)	80 / 92 (87.0)
>= 65	10 / 10 (100)	10 / 11 (90.9)	20 / 21 (95.2)
Age Group 2			
<59	24 / 31 (77.4)	21 / 21 (100)	45 / 52 (86.5)
>=59	26 / 29 (89.7)	29 / 32 (90.6)	55 / 61 (90.2)
HCV RNA BSL <800K			
<800K	24 / 27 (88.9)	6 / 6 (100)	30 / 33 (90.9)
>=800K	26 / 33 (78.8)	44 / 47 (93.6)	70 / 80 (87.5)
HCV RNA BSL <2,000K			
<2,000K	31 / 37 (83.8)	10 / 10 (100)	41 / 47 (87.2)
>=2,000K	19 / 23 (82.6)	40 / 43 (93.0)	59 / 66 (89.4)
HCV RNA BSL <6,000K			
<6,000K	20 / 22 (90.9)	6 / 6 (100)	26 / 28 (92.9)
>=6,000K	30 / 38 (78.9)	44 / 47 (93.6)	74 / 85 (87.1)
HCV RNA BSL Categories			
<8000K	24 / 27 (88.9)	6 / 6 (100)	30 / 33 (90.9)
>=10,000K, <12,	. / 2 (0.00)	. / . (.)	. / . (.)
>=12,000K	1 / 1 (100)	12 / 12 (100)	13 / 13 (100)
>=2,000K, <4,00	12 / 14 (85.7)	11 / 12 (91.7)	23 / 26 (88.5)
>=4,000K, <6,00	4 / 4 (100)	8 / 9 (88.9)	12 / 13 (92.3)
>=6,000K, <8,00	2 / 2 (100)	4 / 5 (80.0)	6 / 7 (85.7)
>=8,000K, <10,0	. / . (.)	5 / 5 (100)	5 / 5 (100)
>=800K, <2,000K	7 / 10 (70.0)	4 / 4 (100)	11 / 14 (78.6)
HCV Genotype			
1A	26 / 34 (76.5)	30 / 31 (96.8)	56 / 65 (86.2)
1B	11 / 11 (100)	9 / 10 (90.0)	20 / 21 (95.2)
2	4 / 5 (80.0)	. / . (.)	4 / 5 (80.0)

3	5 / 6 (83.3)	10 / 11 (90.9)	15 / 17 (88.2)
4	4 / 4 (100)	. / . (.)	4 / 4 (100)
6 C-L	. / . (.)	1 / 1 (100)	1 / 1 (100)
BMI category			
25<=, <30	22 / 28 (78.6)	26 / 27 (96.3)	48 / 55 (87.3)
<=25	13 / 13 (100)	8 / 8 (100)	21 / 21 (100)
>=30	15 / 19 (78.9)	16 / 18 (88.9)	31 / 37 (83.8)
MELD Score Category at Baseline			
<15	34 / 39 (87.2)	. / . (.)	34 / 39 (87.2)
>=15	16 / 21 (76.2)	. / . (.)	16 / 21 (76.2)
IL28B Genotype			
CC	13 / 13 (100)	13 / 13 (100)	26 / 26 (100)
CT	28 / 33 (84.8)	28 / 31 (90.3)	56 / 64 (87.5)
TT	9 / 14 (64.3)	9 / 9 (100)	18 / 23 (78.3)
Fibrosis Score Category			
F0	. / . (.)	6 / 6 (100)	6 / 6 (100)
F1	1 / 1 (100)	10 / 10 (100)	11 / 11 (100)
F2	2 / 3 (66.7)	7 / 7 (100)	9 / 10 (90.0)
F3	6 / 8 (75.0)	12 / 13 (92.3)	18 / 21 (85.7)
F4	41 / 48 (85.4)	15 / 16 (93.8)	56 / 64 (87.5)
Fibrosis Score Category -- 1			
F0 - F2	3 / 4 (75.0)	23 / 23 (100)	26 / 27 (96.3)
F3 - F4	47 / 56 (83.9)	27 / 29 (93.1)	74 / 85 (87.1)
missing	. / . (.)	. / 1 (0.00)	. / . (.)
Fibrosis Score Category -- 2			
F0 - F3	9 / 12 (75.0)	35 / 36 (97.2)	44 / 48 (91.7)
F4	41 / 48 (85.4)	15 / 16 (93.8)	56 / 64 (87.5)
missing	. / . (.)	. / 1 (0.00)	. / . (.)
Child-Pugh Score Category			
A	11 / 12 (91.7)	. / . (.)	11 / 12 (91.7)
B	30 / 32 (93.8)	. / . (.)	30 / 32 (93.8)
C	9 / 16 (56.3)	. / . (.)	9 / 16 (56.3)
Prior Treatment			
INTERFERON	1 / 1 (100)	. / . (.)	1 / 1 (100)
INTERFERON/RIBA	25 / 32 (78.1)	22 / 24 (91.7)	47 / 56 (83.9)
OTHER	. / . (.)	1 / 1 (100)	1 / 1 (100)
PEGIFN/RIBAVIRI	1 / 2 (50.0)	1 / 1 (100)	2 / 3 (66.7)
PEGIFN/RIBAVIRI	1 / 1 (100)	5 / 5 (100)	6 / 6 (100)
Prior Response Category			
	22 / 24 (91.7)	21 / 22 (95.5)	43 / 46 (93.5)
BREAKTHROUGH	. / . (.)	3 / 3 (100)	3 / 3 (100)
HCV RNA NEVER U	1 / 1 (100)	2 / 2 (100)	3 / 3 (100)
INDETERMINATE	6 / 9 (66.7)	5 / 5 (100)	11 / 14 (78.6)
INTOLERANCE	4 / 7 (57.1)	3 / 4 (75.0)	7 / 11 (63.6)
NULL RESPONDER	8 / 10 (80.0)	5 / 5 (100)	13 / 15 (86.7)
PARTIAL RESPOND	2 / 2 (100)	2 / 2 (100)	4 / 4 (100)

RELAPSER	7 / 7 (100)	9 / 10 (90.0)	16 / 17 (94.1)
Country			
USA	50 / 60 (83.3)	50 / 53 (94.3)	100 /113 (88.5)

Table 27: Subgroup Analyses of SVR12 GT-1 Subjects Only for Study AI444216 (Treated Subjects)

Efficacy Parameter	TN	TE	Total
Treated (ITT)			
N	80/ 83 (96.4)	43/ 44 (97.7)	123/127 (96.9)
Gender			
FEMALE	6 / 7 (85.7)	7 / 7 (100)	13 / 14 (92.9)
MALE	74 / 76 (97.4)	36 / 37 (97.3)	110 /113 (97.3)
Race			
WHITE	48 / 51 (94.1)	24 / 24 (100)	72 / 75 (96.0)
BLACK/AFRICAN A AMERICAN	27 / 27 (100)	18 / 19 (94.7)	45 / 46 (97.8)
AMERICAN INDIAN/ALASKA NATIVE	2 / 2 (100)	1 / 1 (100)	3 / 3 (100)
ASIAN OTHER	1 / 1 (100)	. / . (.)	1 / 1 (100)
OTHER	2 / 2 (100)	. / . (.)	2 / 2 (100)
Ethnicity			
HISPANIC/LATINO	14 / 14 (100)	8 / 8 (100)	22 / 22 (100)
NOT HISPANIC/LATINO	66 / 69 (95.7)	35 / 36 (97.2)	101 /105 (96.2)
Age Group 3			
<=50	34 / 36 (94.4)	11 / 11 (100)	45 / 47 (95.7)
>50	46 / 47 (97.9)	32 / 33 (97.0)	78 / 80 (97.5)
Age Group 1			
< 65	75 / 78 (96.2)	41 / 42 (97.6)	116 /120 (96.7)
>= 65	5 / 5 (100)	2 / 2 (100)	7 / 7 (100)
Age Group 2			
<65	75 / 78 (96.2)	41 / 42 (97.6)	116 /120 (96.7)
>=65, <75	5 / 5 (100)	2 / 2 (100)	7 / 7 (100)
Age Group 4			
<40	9 / 11 (81.8)	. / . (.)	9 / 11 (81.8)
40-50	23 / 23 (100)	10 / 10 (100)	33 / 33 (100)
50-60	33 / 34 (97.1)	21 / 22 (95.5)	54 / 56 (96.4)
>=60	15 / 15 (100)	12 / 12 (100)	27 / 27 (100)
HCV RNA BSL <800K			
<800K	16 / 16 (100)	6 / 6 (100)	22 / 22 (100)
>=800K	64 / 67 (95.5)	37 / 38 (97.4)	101 /105 (96.2)
HCV RNA BSL <2,000K			
<2,000K	27 / 29 (93.1)	13 / 13 (100)	40 / 42 (95.2)
>=2,000K	53 / 54 (98.1)	30 / 31 (96.8)	83 / 85 (97.6)

HCV RNA BSL <6,000K			
<6,000K	56 / 58 (96.6)	33 / 33 (100)	89 / 91 (97.8)
>=6,000K	42 / 43 (97.7)	18 / 19 (94.7)	60 / 62 (96.8)
HCV RNA BSL Categories			
<8000K	16 / 16 (100)	6 / 6 (100)	22 / 22 (100)
>=8000K, <2,000K	11 / 13 (84.6)	7 / 7 (100)	18 / 20 (90.0)
>=2,000K, <4,000K	9 / 9 (100)	6 / 6 (100)	15 / 15 (100)
>=4,000K, <6,000K	12 / 12 (100)	9 / 9 (100)	21 / 21 (100)
>=6,000K, <8,000K	7 / 7 (100)	3 / 3 (100)	10 / 10 (100)
>=8,000K, <10,000K	3 / 3 (100)	3 / 3 (100)	6 / 6 (100)
>=10,000K, <12,000K	5 / 6 (83.3)	2 / 2 (100)	7 / 8 (87.5)
>=12,000K	17 / 17 (100)	7 / 8 (87.5)	24 / 25 (96.0)
HCV Genotype			
1A	68 / 71 (95.8)	32 / 33 (97.0)	100 /104 (96.2)
1B	12 / 12 (100)	11 / 11 (100)	23 / 23 (100)
BMI category			
<=25	34 / 37 (91.9)	13 / 14 (92.9)	47 / 51 (92.2)
25<=, <30	34 / 34 (100)	21 / 21 (100)	55 / 55 (100)
>=30	12 / 12 (100)	9 / 9 (100)	21 / 21 (100)
Baseline Cirrhosis Category			
YES	8 / 9 (88.9)	12 / 13 (92.3)	20 / 22 (90.9)
NO	70 / 72 (97.2)	28 / 28 (100)	98 /100 (98.0)
.	2 / 2 (100)	3 / 3 (100)	5 / 5 (100)
HIV RNA Category at Baseline			
<500K	80 / 83 (96.4)	43 / 44 (97.7)	123 /127 (96.9)
IL28B Genotype			
CC	20 / 20 (100)	9 / 9 (100)	29 / 29 (100)
CT	38 / 41 (92.7)	25 / 26 (96.2)	63 / 67 (94.0)
TT	22 / 22 (100)	9 / 9 (100)	31 / 31 (100)
Fibrosis Score Category			
F0	22 / 24 (91.7)	8 / 8 (100)	30 / 32 (93.8)
F1	23 / 23 (100)	9 / 9 (100)	32 / 32 (100)
F2	10 / 10 (100)	7 / 7 (100)	17 / 17 (100)
F3	19 / 19 (100)	9 / 10 (90.0)	28 / 29 (96.6)
F4	21 / 22 (95.5)	18 / 18 (100)	39 / 40 (97.5)
missing	3 / 3 (100)	. / . (.)	3 / 3 (100)
Fibrosis Score Category -- 1			
F0 - F2	55 / 57 (96.5)	24 / 24 (100)	79 / 81 (97.5)
F3 - F4	40 / 41 (97.6)	27 / 28 (96.4)	67 / 69 (97.1)
missing	3 / 3 (100)	. / . (.)	3 / 3 (100)
Fibrosis Score Category -- 2			
F0 - F3	57 / 59 (96.6)	26 / 27 (96.3)	83 / 86 (96.5)
F4	20 / 21 (95.2)	17 / 17 (100)	37 / 38 (97.4)
missing	3 / 3 (100)	. / . (.)	3 / 3 (100)
CD4 Category at Baseline --1			

<200	4 / 4 (100)	. / . (.)	4 / 4 (100)
>=200	76 / 79 (96.2)	43 / 43 (100)	119 /122 (97.5)
CD4 Category at Baseline --2			
< 200	4 / 4 (100)	. / . (.)	4 / 4 (100)
200 - < 500	31 / 32 (96.9)	11 / 11 (100)	42 / 43 (97.7)
>= 500	45 / 47 (95.7)	32 / 32 (100)	77 / 79 (97.5)
cART Regimen			
PI	40 / 41 (97.6)	21 / 22 (95.5)	61 / 63 (96.8)
NNRTI	20 / 20 (100)	10 / 10 (100)	30 / 30 (100)
OTHER	20 / 22 (90.9)	12 / 12 (100)	32 / 34 (94.1)
cART Individual			
ATAZANAVIR	17 / 17 (100)	12 / 12 (100)	29 / 29 (100)
DARUNAVIR	14 / 15 (93.3)	9 / 10 (90.0)	23 / 25 (92.0)
EFAVIRENZ	13 / 13 (100)	7 / 7 (100)	20 / 20 (100)
LOPINAVIR	9 / 9 (100)	. / . (.)	9 / 9 (100)
NEVIRAPINE	5 / 5 (100)	2 / 2 (100)	7 / 7 (100)
RILPIVIRINE	2 / 2 (100)	1 / 1 (100)	3 / 3 (100)
Prior Treatment			
INTERFERON/RIBAVIRIN	1 / 1 (100)	30 / 31 (96.8)	31 / 32 (96.9)
PEGIFN/RIBAVIRIN/BOC	. / . (.)	5 / 5 (100)	5 / 5 (100)
PEGIFN/RIBAVIRIN/TRV	. / . (.)	5 / 5 (100)	5 / 5 (100)
SOFOSBUVIR/RIBAVIRIN	. / . (.)	1 / 1 (100)	1 / 1 (100)
INTERFERON	. / . (.)	1 / 1 (100)	1 / 1 (100)
OTHER	. / . (.)	1 / 1 (100)	1 / 1 (100)
Prior Response Category			
NULL RESPONDER	1 / 1 (100)	14 / 15 (93.3)	15 / 16 (93.8)
RELAPSER	. / . (.)	10 / 10 (100)	10 / 10 (100)
INTOLERANCE	. / . (.)	8 / 8 (100)	8 / 8 (100)
PARTIAL RESPONDER	. / . (.)	7 / 7 (100)	7 / 7 (100)
INDETERMINATE	. / . (.)	2 / 2 (100)	2 / 2 (100)
BREAKTHROUGH	. / . (.)	1 / 1 (100)	1 / 1 (100)
HCV RNA NEVER UNDETECTABLE ON TREATMENT	. / . (.)	1 / 1 (100)	1 / 1 (100)
DCV Dose Category			
30 MG	40 / 41 (97.6)	21 / 22 (95.5)	61 / 63 (96.8)
60 MG	22 / 24 (91.7)	13 / 13 (100)	35 / 37 (94.6)
90 MG	18 / 18 (100)	9 / 9 (100)	27 / 27 (100)
Country			
USA	80 / 83 (96.4)	43 / 44 (97.7)	123 /127 (96.9)

Table 28: Subgroup Analyses of SVR12 GT-3 Subjects for Study AI444216 (Treated Subjects)

Efficacy Parameter	TN	TE	Total
Treated (ITT)			
N	6 / . (100)	4 / . (100)	10 / . (.)
Gender			
FEMALE	. / . (.)	2 / 2 (100)	2 / 2 (100)
MALE	6 / 6 (100)	2 / 2 (100)	8 / 8 (100)
Race			
BLACK/AFRICAN A	1 / 1 (100)	1 / 1 (100)	2 / 2 (100)
WHITE	5 / 5 (100)	3 / 3 (100)	8 / 8 (100)
Ethnicity			
HISPANIC/LATINO	. / . (.)	1 / 1 (100)	1 / 1 (100)
NOT HISPANIC/LA	6 / 6 (100)	3 / 3 (100)	9 / 9 (100)
Age Group 1			
< 65	6 / 6 (100)	3 / 3 (100)	9 / 9 (100)
>= 65	. / . (.)	1 / 1 (100)	1 / 1 (100)
Age Group 2			
<65	6 / 6 (100)	3 / 3 (100)	9 / 9 (100)
>=65, <75	. / . (.)	1 / 1 (100)	1 / 1 (100)
Age Group 3			
<=50	3 / 3 (100)	. / . (.)	3 / 3 (100)
>50	3 / 3 (100)	4 / 4 (100)	7 / 7 (100)
Age Group 4			
40-50	3 / 3 (100)	. / . (.)	3 / 3 (100)
50-60	3 / 3 (100)	1 / 1 (100)	4 / 4 (100)
>=60	. / . (.)	3 / 3 (100)	3 / 3 (100)
HCV RNA BSL <2,000K			
<2,000K	2 / 2 (100)	3 / 3 (100)	5 / 5 (100)
>=2,000K	4 / 4 (100)	1 / 1 (100)	5 / 5 (100)
HCV RNA BSL <6,000K			
<6,000K	3 / 3 (100)	3 / 3 (100)	6 / 6 (100)
>=6,000K	3 / 3 (100)	1 / 1 (100)	4 / 4 (100)
HCV RNA BSL Categories			
<8000K	2 / 2 (100)	2 / 2 (100)	4 / 4 (100)
>=10,000K, <12,	1 / 1 (100)	. / . (.)	1 / 1 (100)
>=12,000K	. / . (.)	1 / 1 (100)	1 / 1 (100)
>=4,000K, <6,00	1 / 1 (100)	. / . (.)	1 / 1 (100)
>=6,000K, <8,00	1 / 1 (100)	. / . (.)	1 / 1 (100)
>=8,000K, <10,0	1 / 1 (100)	. / . (.)	1 / 1 (100)
>=800K, <2,000K	. / . (.)	1 / 1 (100)	1 / 1 (100)
HCV Genotype			
3	6 / 6 (100)	4 / 4 (100)	10 / 10 (100)

BMI category				
<=25	5 / 5 (100)	2 / 2 (100)	7 / 7 (100)	
>=30	1 / 1 (100)	2 / 2 (100)	3 / 3 (100)	
Baseline Cirrhosis Category				
NO	6 / 6 (100)	3 / 3 (100)	9 / 9 (100)	
YES	. / . (.)	1 / 1 (100)	1 / 1 (100)	
IL28B Genotype				
CC	2 / 2 (100)	1 / 1 (100)	3 / 3 (100)	
CT	3 / 3 (100)	3 / 3 (100)	6 / 6 (100)	
TT	1 / 1 (100)	. / . (.)	1 / 1 (100)	
Fibrosis Score Category				
F0	1 / 1 (100)	. / . (.)	1 / 1 (100)	
F1	3 / 3 (100)	1 / 1 (100)	4 / 4 (100)	
F2	2 / 2 (100)	2 / 2 (100)	4 / 4 (100)	
F3	. / . (.)	1 / 1 (100)	1 / 1 (100)	
Fibrosis Score Category -- 1				
F0 - F2	6 / 6 (100)	3 / 3 (100)	9 / 9 (100)	
F3 - F4	. / . (.)	1 / 1 (100)	1 / 1 (100)	
Fibrosis Score Category -- 2				
F0 - F3	6 / 6 (100)	4 / 4 (100)	10 / 10 (100)	
CD4 Category at Baseline --1				
>=200	6 / 6 (100)	4 / 4 (100)	10 / 10 (100)	
CD4 Category at Baseline --2				
200 - < 500	4 / 4 (100)	. / . (.)	4 / 4 (100)	
>= 500	2 / 2 (100)	4 / 4 (100)	6 / 6 (100)	
cART Individual				
DARUNAVIR	3 / 3 (100)	1 / 1 (100)	4 / 4 (100)	
EFAVIRENZ	1 / 1 (100)	1 / 1 (100)	2 / 2 (100)	
RILPIVIRINE	2 / 2 (100)	. / . (.)	2 / 2 (100)	
Prior Treatment				
INTERFERON/RIBA	. / . (.)	2 / 2 (100)	2 / 2 (100)	
SOFOBUVIR/RIBA	. / . (.)	2 / 2 (100)	2 / 2 (100)	
Prior Response Category				
BREAKTHROUGH	6 / 6 (100)	. / . (.)	6 / 6 (100)	
NULL RESPONDER	. / . (.)	1 / 1 (100)	1 / 1 (100)	
RELAPSER	. / . (.)	1 / 1 (100)	1 / 1 (100)	
RELAPSER				
	. / . (.)	2 / 2 (100)	2 / 2 (100)	
DCV Dose Category				
30 MG	3 / 3 (100)	1 / 1 (100)	4 / 4 (100)	
60 MG	2 / 2 (100)	2 / 2 (100)	4 / 4 (100)	
90 MG	1 / 1 (100)	1 / 1 (100)	2 / 2 (100)	
Country				
USA	6 / 6 (100)	4 / 4 (100)	10 / 10 (100)	

Table 29: Subgroup Analyses of SVR12 All Subjects for Study AI444216 (Treated Subjects)

Efficacy Parameter	TN	TE	Total
Treated (ITT)			
N	98/101 (97.0)	51/ 52 (98.1)	149/153 (97.4)
Gender			
FEMALE	8 / 9 (88.9)	9 / 9 (100)	17 / 18 (94.4)
MALE	90 / 92 (97.8)	42 / 43 (97.7)	132 /135 (97.8)
Race			
WHITE	63 / 66 (95.5)	31 / 31 (100)	94 / 97 (96.9)
BLACK/AFRICAN AMERICAN	30 / 30 (100)	19 / 20 (95.0)	49 / 50 (98.0)
AMERICAN INDIAN/ALASKA NATIVE	2 / 2 (100)	1 / 1 (100)	3 / 3 (100)
ASIAN OTHER	1 / 1 (100)	. / . (.)	1 / 1 (100)
OTHER	2 / 2 (100)	. / . (.)	2 / 2 (100)
Ethnicity			
HISPANIC/LATINO	18 / 18 (100)	10 / 10 (100)	28 / 28 (100)
NOT HISPANIC/LATINO	80 / 83 (96.4)	41 / 42 (97.6)	121 /125 (96.8)
Age Group (Median Age)			
<=50	43 / 45 (95.6)	12 / 12 (100)	55 / 57 (96.5)
>50	55 / 56 (98.2)	39 / 40 (97.5)	94 / 96 (97.9)
Age Group 1 (all failure are less than 65 years old)			
< 65	93 / 96 (96.9)	48 / 49 (98.0)	141 /145 (97.2)
>= 65	5 / 5 (100)	3 / 3 (100)	8 / 8 (100)
Age Group 2			
<65	93 / 96 (96.9)	48 / 49 (98.0)	141 /145 (97.2)
>=65, <75	5 / 5 (100)	3 / 3 (100)	8 / 8 (100)
Age Group 3			
<40	10 / 12 (83.3)	. / . (.)	10 / 12 (83.3)
40-50	30 / 30 (100)	11 / 11 (100)	41 / 41 (100)
50-60	43 / 44 (97.7)	24 / 25 (96.0)	67 / 69 (97.1)
>=60	15 / 15 (100)	16 / 16 (100)	31 / 31 (100)
HCV RNA BSL <800K			
<800K	22 / 22 (100)	8 / 8 (100)	30 / 30 (100)
>=800K	76 / 79 (96.2)	43 / 44 (97.7)	119 /123 (96.7)
HCV RNA BSL <2,000K			
<2,000K	33 / 35 (94.3)	17 / 17 (100)	50 / 52 (96.2)
>=2,000K	65 / 66 (98.5)	34 / 35 (97.1)	99 /101 (98.0)
HCV RNA BSL <6,000K			
<6,000K	56 / 58 (96.6)	33 / 33 (100)	89 / 91 (97.8)
>=6,000K	42 / 43 (97.7)	18 / 19 (94.7)	60 / 62 (96.8)
HCV RNA BSL Categories			
<8000K	22 / 22 (100)	8 / 8 (100)	30 / 30 (100)

>=8000K, <2,000K	11 / 13 (84.6)	9 / 9 (100)	20 / 22 (90.9)
>=2,000K, <4,000K	10 / 10 (100)	7 / 7 (100)	17 / 17 (100)
>=4,000K, <6,000K	13 / 13 (100)	9 / 9 (100)	22 / 22 (100)
>=6,000K, <8,000K	8 / 8 (100)	3 / 3 (100)	11 / 11 (100)
>=8,000K, <10,000K	5 / 5 (100)	3 / 3 (100)	8 / 8 (100)
>=10,000K, <12,000K	7 / 8 (87.5)	2 / 2 (100)	9 / 10 (90.0)
>=12,000K	22 / 22 (100)	10 / 11 (90.9)	32 / 33 (97.0)
HCV Genotype	(all failure are GT-1a)		
1A	68 / 71 (95.8)	32 / 33 (97.0)	100 /104 (96.2)
1B	12 / 12 (100)	11 / 11 (100)	23 / 23 (100)
2	11 / 11 (100)	2 / 2 (100)	13 / 13 (100)
3	6 / 6 (100)	4 / 4 (100)	10 / 10 (100)
4	1 / 1 (100)	2 / 2 (100)	3 / 3 (100)
BMI category	(all failure have BMI less or equal to 25)		
<=25	47 / 50 (94.0)	16 / 17 (94.1)	63 / 67 (94.0)
25<=, <30	37 / 37 (100)	22 / 22 (100)	59 / 59 (100)
>=30	14 / 14 (100)	13 / 13 (100)	27 / 27 (100)
Baseline Cirrhosis Category			
YES	8 / 9 (88.9)	14 / 15 (93.3)	22 / 24 (91.7)
NO	88 / 90 (97.8)	34 / 34 (100)	122 /124 (98.4)
.	2 / 2 (100)	3 / 3 (100)	5 / 5 (100)
HIV RNA Category at Baseline			
<500K	98 /101 (97.0)	51 / 52 (98.1)	149 /153 (97.4)
IL28B Genotype			
CC	28 / 28 (100)	13 / 13 (100)	41 / 41 (100)
CT	45 / 48 (93.8)	29 / 30 (96.7)	74 / 78 (94.9)
TT	25 / 25 (100)	9 / 9 (100)	34 / 34 (100)
Fibrosis Score Category			
F0	22 / 24 (91.7)	8 / 8 (100)	30 / 32 (93.8)
F1	23 / 23 (100)	9 / 9 (100)	32 / 32 (100)
F2	10 / 10 (100)	7 / 7 (100)	17 / 17 (100)
F3	19 / 19 (100)	9 / 10 (90.0)	28 / 29 (96.6)
F4	21 / 22 (95.5)	18 / 18 (100)	39 / 40 (97.5)
missing	3 / 3 (100)	. / . (.)	3 / 3 (100)
Fibrosis Score Category -- 1			
F0 - F2	55 / 57 (96.5)	24 / 24 (100)	79 / 81 (97.5)
F3 - F4	40 / 41 (97.6)	27 / 28 (96.4)	67 / 69 (97.1)
missing	3 / 3 (100)	. / . (.)	3 / 3 (100)
Fibrosis Score Category -- 2			
F0 - F3	74 / 76 (97.4)	33 / 34 (97.1)	107 /110 (97.3)
F4	21 / 22 (95.5)	18 / 18 (100)	39 / 40 (97.5)
missing	3 / 3 (100)	. / . (.)	3 / 3 (100)
CD4 Category at Baseline --1			
<200	4 / 4 (100)	. / . (.)	4 / 4 (100)
>=200	94 / 97 (96.9)	51 / 51 (100)	145 /148 (98.0)

CD4 Category at Baseline --2			
< 200	4 / 4 (100)	. / . (.)	4 / 4 (100)
200 - < 500	41 / 42 (97.6)	12 / 12 (100)	53 / 54 (98.1)
>= 500	53 / 55 (96.4)	39 / 39 (100)	92 / 94 (97.9)
cART Regimen			
PI	46 / 47 (97.9)	22 / 23 (95.7)	68 / 70 (97.1)
NNRTI	28 / 28 (100)	12 / 12 (100)	40 / 40 (100)
NONE	1 / 1 (100)	1 / 1 (100)	2 / 2 (100)
OTHER	23 / 25 (92.0)	16 / 16 (100)	39 / 41 (95.1)
cART Individual			
ATAZANAVIR	19 / 19 (100)	12 / 12 (100)	31 / 31 (100)
DARUNAVIR	18 / 19 (94.7)	10 / 11 (90.9)	28 / 30 (93.3)
EFAVIRENZ	18 / 18 (100)	8 / 8 (100)	26 / 26 (100)
LOPINAVIR	9 / 9 (100)	. / . (.)	9 / 9 (100)
NEVIRAPINE	5 / 5 (100)	3 / 3 (100)	8 / 8 (100)
RILPIVIRINE	5 / 5 (100)	1 / 1 (100)	6 / 6 (100)
Prior Treatment			
INTERFERON/RIBAVIRIN	1 / 1 (100)	36 / 37 (97.3)	37 / 38 (97.4)
PEGIFN/RIBAVIRIN/BOC	. / . (.)	5 / 5 (100)	5 / 5 (100)
PEGIFN/RIBAVIRIN/TRV	. / . (.)	5 / 5 (100)	5 / 5 (100)
SOFOSBUVIR/RIBAVIRIN	. / . (.)	3 / 3 (100)	3 / 3 (100)
INTERFERON	. / . (.)	1 / 1 (100)	1 / 1 (100)
OTHER	. / . (.)	1 / 1 (100)	1 / 1 (100)
Prior Response Category			
NULL RESPONDER	1 / 1 (100)	16 / 17 (94.1)	17 / 18 (94.4)
RELAPSER	. / . (.)	14 / 14 (100)	14 / 14 (100)
INTOLERANCE	. / . (.)	8 / 8 (100)	8 / 8 (100)
PARTIAL RESPONDER	. / . (.)	7 / 7 (100)	7 / 7 (100)
INDETERMINATE	. / . (.)	3 / 3 (100)	3 / 3 (100)
BREAKTHROUGH	. / . (.)	2 / 2 (100)	2 / 2 (100)
HCV RNA NEVER UNDETECTABLE ON TREATMENT	. / . (.)	1 / 1 (100)	1 / 1 (100)
DCV Dose Category			
30 MG	46 / 47 (97.9)	22 / 23 (95.7)	68 / 70 (97.1)
60 MG	29 / 31 (93.5)	18 / 18 (100)	47 / 49 (95.9)
90 MG	23 / 23 (100)	11 / 11 (100)	34 / 34 (100)
Country			
USA	98 /101 (97.0)	51 / 52 (98.1)	149 /153 (97.4)

References

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

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/s/

WEN ZENG
01/20/2016

THAMBAN I VALAPPIL
01/20/2016