Clinical trial results:
An Open-Label Study to Explore the Clinical Efficacy of GS-7977 with Ribavirin Administered Pre-Transplant in Preventing Hepatitis C Virus (HCV) Recurrence Post-Transplant

Summary

EudraCT number	2012-000637-39
Trial protocol	ES
Global end of trial date	20 October 2014

Results information

Result version number	v1 (current)
This version publication date	02 July 2016
First version publication date	02 July 2016

Trial information

Trial identification

Sponsor protocol code	P7977-2025

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01559844
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com
Scientific contact	Clinical Trial Mailbox, Gilead Sciences International Ltd, ClinicalTrialDisclosures@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine if the administration of a combination of sofosbuvir (SOF; GS-7977) and ribavirin (RBV) to HCV-infected subjects with hepatocellular carcinoma (HCC) meeting the MILAN criteria prior to undergoing liver transplantation could prevent post-transplant re-infection as determined by a sustained post-transplant virological response (HCV RNA < lower limit of quantitation [LLOQ]) at 12 weeks post-transplant.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 March 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	United States: 55
Worldwide total number of subjects	61
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	53
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States, Spain, and New Zealand. The first participant was screened on 27 March 2012. The last study visit occurred on 20 October 2014.

Pre-assignment

Screening details:

92 participants were screened.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	SOF+RBV

Arm description:

SOF+RBV for up to 48 weeks or until time of transplant, whichever occured first.

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir
Investigational medicinal product code	
Other name	Sovaldi®, GS-7977
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Sofosbuvir (SOF) 400 mg administered once daily

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin (RBV) administered in a divided daily dose based on weight (< 75kg = 1000 mg and ≥ 75 kg = 1200 mg)

Number of subjects in period 1	SOF+RBV
Started	61
Completed	36
Not completed	25
Death	5
Efficacy Failure	10
No Longer A Transplant Candidate	3
Consent Withdrawn	7

Baseline characteristics

Reporting groups	
Reporting group title	SOF+RBV
Reporting group description:	
SOF+RBV for up to 48 weeks or until time of transplant, whichever occured first.	

Reporting group values	SOF+RBV	Total	
Number of subjects	61	61	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	59		
standard deviation	± 5.5	-	
Gender categorical Units: Subjects			
Female	12	12	
Male	49	49	
Ethnicity Units: Subjects			
Hispanic or Latino	12	12	
Not Hispanic or Latino	49	49	
Race Units: Subjects			
White	55	55	
Black or African American	6	6	
Prior Hepatitis C Virus (HCV) Treatment Units: Subjects			
Yes	46	46	
No	15	15	
Response to Last Prior HCV Treatment Regimen Units: Subjects			
Non-Responder: Null	11	11	
Non-Responder: Partial	11	11	
Responder: Breakthrough	3	3	
Responder: Relapser	9	9	
Unknown	12	12	
Had Not Received Prior Treatment	15	15	
Baseline HCV RNA Category Units: Subjects			
< 6 log10 IU/mL	20	20	
≥ 6 and < 7 log10 IU/mL	38	38	
≥ 7 log10 IU/mL	3	3	
HCV Genotype			
There are variations of HCV which are all similar enough to be called HCV, but are distinct enough to be referred to as HCV genotypes.			

Units: Subjects			
Genotype 1a	24	24	
Genotype 1b	21	21	
Genotype 2a	1	1	
Genotype 2b	7	7	
Genotype 3a	7	7	
Genotype 4a	1	1	
IL28b Status			
CC, CT, and TT alleles are different forms of the IL28b gene.			
Units: Subjects			
CC	13	13	
CT	39	39	
TT	8	8	
Missing	1	1	
Baseline Child-Pugh Turcotte (CPT) Score			
CPT scores, widely used to grade the severity of cirrhosis and to determine the need for liver transplantation, are calculated based on a combination of laboratory values and clinical features. CPT scores can range from 5 to 15, with higher scores indicating a greater severity of disease.			
Units: Subjects			
CPT Score = 5	26	26	
CPT Score = 6	18	18	
CPT Score = 7	14	14	
CPT Score = 8	3	3	
Baseline Model For End-Stage Liver Disease (MELD) Score			
MELD scores, used to assess prognosis and suitability for transplant, are calculated based on laboratory values only and can range from 6 to 40, with higher scores indicating greater disease severity.			
Units: Subjects			
MELD Score = 6	5	5	
MELD Score = 7	18	18	
MELD Score = 8	12	12	
MELD Score = 9	9	9	
MELD Score = 10	6	6	
MELD Score = 11	8	8	
MELD Score = 13	2	2	
MELD Score = 14	1	1	
Days on Transplant Waitlist			
Units: days			
arithmetic mean	266		
standard deviation	± 488.8	-	
Baseline HCV RNA			
Units: log10 IU/mL			
arithmetic mean	6.14		
standard deviation	± 0.633	-	

End points

End points reporting groups

Reporting group title	SOF+RBV
Reporting group description:	
SOF+RBV for up to 48 weeks or until time of transplant, whichever occured first.	

Primary: Percentage of Participants With Posttransplant Virologic Response (pTVR) at Posttransplant Week 12

End point title	Percentage of Participants With Posttransplant Virologic Response (pTVR) at Posttransplant Week 12[1]
End point description:	
pTVR was defined as HCV RNA < the lower limit of quantification (LLOQ, ie, 25 mL/IU) at Week 12 after transplant. Participants in the Full Analysis Set (enrolled and received at least 1 dose of study drug) who underwent liver transplantation, and who had HCV RNA < LLOQ at last measurement prior to transplant were analyzed.	
End point type	Primary
End point timeframe:	
Posttransplant Week 12	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	SOF+RBV			
Subject group type	Reporting group			
Number of subjects analysed	43[2]			
Units: percentage of participants				
number (not applicable)				
Transplant after ≥ 12 weeks of treatment (n=32)	75			
Transplant after any duration of treatment (n=43)	69.8			

Notes:

[2] - Participants who had liver transplantation & HCV RNA < LLOQ at last measurement prior to transplant

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Experiencing Any Adverse Event Leading to Permanent Discontinuation of Sofosbuvir Prior to Receiving Transplant

End point title	Percentage of Participants Experiencing Any Adverse Event Leading to Permanent Discontinuation of Sofosbuvir Prior to Receiving Transplant[3]
End point description:	
End point type	Primary

End point timeframe:

Up to 48 weeks prior to transplant

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	SOF+RBV			
Subject group type	Reporting group			
Number of subjects analysed	61[4]			
Units: percentage of participants				
number (not applicable)	3.3			

Notes:

[4] - Safety Analysis Set: participants who were enrolled and received at least 1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Graft Loss Following Transplant

End point title	Percentage of Participants With Graft Loss Following

End point description:

End point type	Primary

End point timeframe:

Up to 48 weeks following transplant

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	SOF+RBV			
Subject group type	Reporting group			
Number of subjects analysed	46[6]			
Units: percentage of participants				
number (not applicable)	6.5			

Notes:

[6] - Participants in the Safety Analysis Set who underwent liver transplantation were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Died

End point title	Number of Participants Who Died[7]

End point description:

• Treatment-emergent deaths were those that occurred while taking study drug or to the minimum of 1) date of transplantation, 2) retreatment 1st dose date, or 3) last dose date + 30 days.
• Only those participants who underwent liver transplantation were analyzed for death post-transplantation.

End point type	Primary

End point timeframe:

Up to 48 weeks following transplant

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	SOF+RBV			
Subject group type	Reporting group			
Number of subjects analysed	61[8]			
Units: participants				
All Deaths	5			
Treatment-Emergent Death (n = 61)	1			
Death Following Transplant (n = 46)	3			
Death Not Meeting Either Criteria (n = 61)	1			

Notes:

[8] - Safety Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Posttransplant Virologic Response (pTVR) Through Posttransplant Week 48

End point title	Percentage of Participants With Posttransplant Virologic Response (pTVR) Through Posttransplant Week 48

End point description:

pTVR was defined as HCV RNA < the lower limit of quantification (LLOQ, ie, 25 mL/IU) at the relevant time point after transplant.

Participants in the Full Analysis Set who underwent liver transplantation and who had ≥ 12 weeks treatment and HCV RNA < LLOQ at last measurement prior to transplant were analyzed.

End point type	Secondary

End point timeframe:

Up to 48 weeks following transplant

End point values	SOF+RBV			
Subject group type	Reporting group			
Number of subjects analysed	32[9]			
Units: percentage of participants				
number (not applicable)				
Posttransplant Week 1 (n = 32)	87.5			
Posttransplant Week 2 (n = 32)	81.3			
Posttransplant Week 4 (n = 32)	75			
Posttransplant Week 8 (n = 32)	75			
Posttransplant Week 24 (n = 32)	75			
Posttransplant Week 48 (n = 30)	66.7			

Notes:

[9] - Had liver transplant, ≥ 12 weeks treatment, & HCV RNA<LLOQ at last measurement before transplant

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With HCV RNA < LLOQ (ie, 25 mL/IU) During Treatment Through Week 48

End point title	Percentage of Participants With HCV RNA < LLOQ (ie, 25 mL/IU) During Treatment Through Week 48

End point description:

End point type	Secondary

End point timeframe:

Up to 48 weeks prior to transplant

End point values	SOF+RBV			
Subject group type	Reporting group			
Number of subjects analysed	61[10]			
Units: percentage of participants				
number (not applicable)				
Week 1 (n = 61)	13.1			
Week 2 (n = 61)	57.4			
Week 3 (n = 60)	81.7			
Week 4 (n = 58)	93.1			
Week 8 (n = 54)	90.7			
Week 12 (n = 48)	93.8			
Week 24 (n = 30)	100			
Week 36 (n = 9)	100			
Week 48 (n = 8)	100			

Notes:

[10] - Participants in the Full Analysis Set with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: HCV RNA and Change From Baseline in HCV RNA Through Week 8

End point title	HCV RNA and Change From Baseline in HCV RNA Through Week 8

End point description:

End point type	Secondary

End point timeframe:

Up to 8 weeks prior to transplant

End point values	SOF+RBV			
Subject group type	Reporting group			
Number of subjects analysed	61[11]			
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Week 1 (n = 59)	-3.87 (± 0.7)			
Week 2 (n = 61)	-4.43 (± 0.771)			
Week 3 (n = 60)	-4.64 (± 0.67)			
Week 4 (n = 58)	-4.69 (± 0.686)			
Week 8 (n = 53)	-4.66 (± 0.708)			

Notes:

[11] - Participants in the Full Analysis Set with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants With Virologic Failure Prior to Transplant

End point title	Proportion of Participants With Virologic Failure Prior to Transplant

End point description:

Virologic failure (VF) in the pretransplant phase was defined by:
• Breakthrough (HCV RNA ≥ 25 IU/ml after having previously had HCV RNA < 25 IU/ml, while on treatment),
• Rebound (breakthrough or > 1 log10 IU/ml increase in HCV RNA from nadir while on treatment),
• Non-response (HCV RNA ≥ 25 IU/ml through 8 weeks of treatment),
• Pre-transplant relapse (HCV RNA ≥ 25 IU/ml during the Pre-Transplant off-treatment follow-up period after having achieved HCV RNA < 25 IU/ml at last observed HCV RNA on treatment).
Analysis Population Descriptions:
On-treatment VF: Full Analysis Set.
Posttreatment/Pretransplant VF - 24 Weeks or 48 Weeks: Participants who completed 24 or 48 weeks of treatment and had an observed or imputed Week 4 posttreatment follow-up HCV RNA value relapsed during posttreatment follow-up were analyzed.

End point type	Secondary

End point timeframe:

Up to 48 weeks prior to transplant

End point values	SOF+RBV			
Subject group type	Reporting group			
Number of subjects analysed	61[12]			
Units: percentage of participants				
number (not applicable)				
On-treatment VF (n = 61)	8.2			

Posttreatment/Pretransplant VF - 24 Weeks (n = 15)	73.3			
Posttreatment/Pretransplant VF - 48 Weeks (n = 8)	37.5			

Notes:

[12] - See End point description for more information on Analysis Population Descriptions.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 48 weeks plus 30 days	
Adverse event reporting additional description:	
Safety Analysis Set	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Reporting groups	
Reporting group title	SOF+RBV
Reporting group description:	
SOF+RBV for up to 48 weeks or until time of transplant, whichever occured first.	

Serious adverse events	SOF+RBV		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 61 (18.03%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatocellular carcinoma			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour thrombosis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Hepatic encephalopathy			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Umbilical hernia, obstructive			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal strangulated hernia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mesenteric artery thrombosis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Vomiting			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc degeneration			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infectious pleural effusion			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peritonitis bacterial			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Sepsis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	SOF+RBV		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 61 (80.33%)		
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 61 (22.95%)		
occurrences (all)	15		
Dizziness			
subjects affected / exposed	4 / 61 (6.56%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	13 / 61 (21.31%)		
occurrences (all)	15		
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	23 / 61 (37.70%) 24 4 / 61 (6.56%) 4		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 10 / 61 (16.39%) 10 6 / 61 (9.84%) 6 4 / 61 (6.56%) 4		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	 7 / 61 (11.48%) 8 7 / 61 (11.48%) 7		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Alopecia subjects affected / exposed occurrences (all)	 9 / 61 (14.75%) 10 6 / 61 (9.84%) 7 4 / 61 (6.56%) 4		
Psychiatric disorders Insomnia			

subjects affected / exposed occurrences (all)	7 / 61 (11.48%) 7		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	 4 / 61 (6.56%) 7		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 4 / 61 (6.56%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 February 2012	The sponsor information was updated to Gilead Sciences, Inc. (Gilead) throughout the document. Section numbers were updated to reflect the Gilead protocol template. The study design and study assessments were clarified. A pharmacogenomic substudy was added to the protocol for subjects who provided their separate and specific consent. The retreatment substudy was added for subjects who experienced posttreatment virologic relapse during the pretransplant treatment phase so they could start a new course of SOF+RBV therapy (after confirmation of no resistance-conferring mutations) for up to an additional 24 weeks of treatment or until transplantation, whichever occurred first. Toxicity management of elevated bilirubin values was added at the request of the US Food and Drug Administration (FDA).
22 March 2012	Updated the monitoring of adverse events (AEs) and serious AEs (SAEs) to occur during the primary treatment period through 30 days after the last dose of study drug. Updated the duration of collection of concomitant medications and vital signs from through posttransplant follow-up Week 48 to 30 days after the last dose of study drug. Updated and clarified reporting requirements and procedures for AEs and SAEs. Added the definition and reporting procedures for special situations. Special situations were defined in the clinical study protocol as pregnancy reports, reports of medication error, abuse, misuse, or overdose, lack of effect reports, reports of adverse reactions in infants following exposure from breastfeeding, and reports of adverse reactions associated with product complaints. However, due to implementation issues, only pregnancy reports and overdose were collected during the study.
21 August 2012	Updated birth control inclusion/exclusion criteria per FDA request. Clarified collection of safety laboratories and assessments 30 days after the last dose of study drug. Updated background information according to available data. Removed requirement for study drug dosing in the clinic on days of study visits after the baseline/Day 1 visit.
22 January 2013	Allowed subjects to continue therapy for up to 48 weeks or until the time of transplant, whichever occurred first. Subjects who had not received a transplant (except those who discontinued study treatment for safety or virologic reasons) at approval of protocol Amendment 4 participated in the pretransplant retreatment phase, which was formerly named the retreatment substudy. Replaced the SOF 200-mg tablets with a single tablet formulation of the SOF 400-mg dose if the supply of 200-mg tablets was depleted. However, the SOF 400-mg tablet was not needed during the study. Removed prohibition of rifaximin (a concomitant medication commonly used to manage the symptoms of hepatic encephalopathy), which is not absorbed when taken orally and, therefore, has a low possibility of interaction with SOF.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

There were no limitations affecting the analysis or results.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25261839