Sofosbuvir in Combination With Pegylated Interferon and Ribavirin and in Treatment-Naive Hepatitis C-infected Patients

This study has been completed.

Sponsor:
Gilead Sciences

ClinicalTrials.gov Identifier:
NCT01188772

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Information provided by (Responsible Party):
Gilead Sciences

Purpose

Genotype 1: Participants with genotype 1 hepatitis C (HCV) infection were randomized to receive **sofosbuvir** (GS-7977; PSI-7977) 200 mg or 400 mg, or matching placebo, plus pegylated interferon alfa 2a (PEG) and ribavirin (RBV) for 12 weeks, followed by PEG+RBV for an up to an additional 36 weeks. Randomization was stratified by IL28B status (CC, CT, TT) and HCV RNA level (< 800,000 IU/ml or ≥ 800,000 IU/ml) at baseline. Participants were randomized in a 2:2:1 manner; those who achieved an extended rapid virologic response (eRVR) (HCV RNA < lower limit of detection [15 IU/mL] from Weeks 4

through 12) received an additional 12 weeks of PEG+RBV. Subjects not achieving eRVR received an additional 36 weeks of PEG+RBV.

Genotype 2 and 3: Participants with genotype 2 or 3 hepatitis C (HCV) received **sofosbuvir** 400 mg plus PEG+RBV for 12 weeks.

Condition	Intervention	Phase
Hepatitis C Virus	Drug: **Sofosbuvir** Drug: Placebo to match **sofosbuvir** Drug: PEG Drug: RBV	**Phase 2**

Study Type: Interventional

Study Design: Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: A Multi-center, Placebo-Controlled, Dose Ranging Study to Investigate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics Following Oral Administration of PSI-7977 in Combination With Pegylated Interferon and Ribavirin in Treatment-Naïve Patients With Chronic HCV Infection Genotype 1, and an Open Label Assessment of PSI-7977 in Patients With HCV Genotypes 2 or 3

Resource links provided by NLM:

MedlinePlus related topics: Hepatitis Hepatitis A Hepatitis C

Drug Information available for: Interferon Ribavirin Sofosbuvir

U.S. FDA Resources

Further study details as provided by Gilead Sciences:

Primary Outcome Measures:

- Percentage of Participants Who Experienced Adverse Events During the **Sofosbuvir** Treatment Period [Time Frame: Baseline to Week 12 plus 30 days]

  Adverse events (AEs) occurring during the sofosbuvir treatment period and for 30 days following the

once if they had a qualifying event.

Secondary Outcome Measures:

- Change in HCV RNA From Baseline to Week 12 [Time Frame: Baseline to Week 12]
- Percentage of Participants With Rapid Virologic Response at Week 4 [Time Frame: Week 4]

  Rapid virologic response was defined as HCV RNA below the limit of detection (< 15 IU/mL) at Week 4 (Day 29)

- Percentage of Participants With Complete Early Virologic Response at Week 12 [Time Frame: Week 12]

  Complete early virologic response was defined as HCV RNA below the limit of detection (< 15 IU/mL) at Week 12

- Percentage of Participants With Extended Rapid Virologic Response [Time Frame: Week 4 to Week 12]

  Extended rapid virologic response was defined as HCV RNA below the limit of detection (< 15 IU/mL) at Week 4 (Day 29) which was maintained through Week 12.

- Percentage of Participants With Virologic Response at the End of Treatment [Time Frame: Week 48 (genotype 1) or Week 12 (genotype 2/3)]

  End-of-treatment virologic response was defined as HCV RNA below the limit of detection (< 15 IU/mL) at the last on-treatment visit.

- Percentage of Participants With Sustained Virologic Response at Post-treatment Week 12 (SVR12) and 24 (SVR24) [Time Frame: Post-treatment Weeks 12 and 24]

  SVR12 and SVR24 were defined as HCV RNA below the limit of detection (< 15 IU/mL) at post-treatment Weeks 12 and 24, respectively.

- Plasma Pharmacokinetics of GS-331007 (Cmax at Day 8) [Time Frame: 1, 2, 4, 8, and 12 hours postdose]

  The pharmacokinetics of sofosbuvir metabolite GS-331007 were analyzed as the maximum observed concentration of drug in plasma (Cmax) at Day 8. Blood samples were collected at 1, 2, and 4 hours postdose for all participants, and at 8 and 12 hours postdose for participants enrolled at selected sites.

- Plasma Pharmacokinetics of GS-331007 (Cmax at Day 15) [Time Frame: 1, 2, 4, 8, and 12 hours postdose]

  The pharmacokinetics of sofosbuvir metabolite GS-331007 were analyzed as the Cmax at Day 15. Blood samples were collected at 1, 2, and 4 hours postdose for all participants, and at 8 and 12 hours postdose for participants enrolled at selected sites.

- Plasma Pharmacokinetics of GS-331007 (Cmax at Day 29) [Time Frame: 1, 2, 4, 8, and 12 hours postdose]

  The pharmacokinetics of sofosbuvir metabolite GS-331007 were analyzed as the Cmax at Day 29. Blood samples were collected at 1, 2, and 4 hours postdose for all participants, and at 8 and 12 hours postdose for participants enrolled at selected sites.

- Plasma Pharmacokinetics of GS-331007 (AUCtau at Day 8) [Time Frame: 1, 2, 4, 8, and 12 hours postdose]

  The pharmacokinetics of sofosbuvir metabolite GS-331007 were analyzed as the the area under the plasma concentration versus time curve over the dosing interval (AUCtau) at Day 8. Blood samples were collected at 1, 2, and 4 hours postdose for all participants, and at 8 and 12 hours postdose for participants enrolled at selected sites.

- Plasma Pharmacokinetics of GS-331007 (AUCtau at Day 15) [Time Frame: 1, 2, 4, 8, and 12 hours postdose]

  The pharmacokinetics of sofosbuvir metabolite GS-331007 were analyzed as the the area under the plasma concentration versus time curve over the dosing interval (AUCtau) at Day 15. Blood samples were collected at 1, 2, and 4 hours postdose for all participants, and at 8 and 12 hours postdose for participants enrolled at selected sites.

- Plasma Pharmacokinetics of GS-331007 (AUCtau at Day 29) [Time Frame: 1, 2, 4, 8, and 12 hours postdose]

  The pharmacokinetics of sofosbuvir metabolite GS-331007 were analyzed as the the area under the plasma concentration versus time curve over the dosing interval (AUCtau) at Day 29. Blood samples were collected at 1, 2, and 4 hours postdose for all participants, and at 8 and 12 hours postdose for participants enrolled at selected sites.

- Percentage of Participants Who Developed Resistance to **Sofosbuvir** [Time Frame: Baseline to Week 12]

  Resistance monitoring was completed in all subjects who received sofosbuvir and who had non-

Enrollment:	147
Study Start Date:	August 2010
Study Completion Date:	May 2012
Primary Completion Date:	April 2011 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: **Sofosbuvir** 200 mg (Genotype 1) Participants with genotype 1 HCV infection were randomized to receive **sofosbuvir** 200 mg (2 x 100 mg tablets)+placebo to match **sofosbuvir** (2 tablets)+PEG+RBV for 12 weeks followed by PEG+RBV for up to an additional 36 weeks.	Drug: **Sofosbuvir** **Sofosbuvir** tablets were administered orally once daily. Other Names: • **Sovaldi®** • GS-7977 • PSI-7977 Drug: Placebo to match **sofosbuvir** Placebo tablets to match **sofosbuvir** were administered orally once daily. Drug: PEG Pegylated interferon alfa-2a (PEG) 180 µg was administered once weekly by subcutaneous injection. Other Name: Pegasys® Drug: RBV Ribavirin (RBV) was administered as a tablet orally according to package insert dosing recommendations (Genotype 1: < 75kg = 1000 mg and ≥ 75 kg = 1200 mg; Genotype 2/3: 800 mg). Other Name: Copegus®
Experimental: **Sofosbuvir** 400 mg (Genotype 1) Participants with genotype 1 HCV infection were randomized to receive **sofosbuvir** 400 mg (4 x 100 mg tablets)+PEG+RBV for 12 weeks followed by PEG+RBV for up to an additional 36 weeks.	Drug: PEG Pegylated interferon alfa-2a (PEG) 180 µg was administered once weekly by subcutaneous injection. Other Name: Pegasys® Drug: RBV

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