ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 07/15/2013

ClinicalTrials.gov ID: NCT00623428

Study Identification

Unique Protocol ID:	MV21371
Brief Title:	A Study of Combination Therapy With PEGASYS (Pegylated Interferon Alfa-2a (40KD)) and Copegus (Ribavirin) in Patients With Chronic Hepatitis C Genotype 2 or 3 Who Do Not Achieve a Rapid Viral Response
Official Title:	A Randomized, Open-label Study of the Effects of 24 vs 48 Weeks of Combination Therapy With PEGASYS (Peginterferon Alfa-2a 40KD) Plus COPEGUS (Ribavirin) on Sustained Virological Response in Patients With Chronic Hepatitis C, Genotype 2 or 3 Who do Not Achieve a Rapid Viral Response
Secondary IDs:	2007-004993-15

Study Status

Record Verification:	July 2013
Overall Status:	Completed
Study Start:	June 2008
Primary Completion:	May 2012 [Actual]
Study Completion:	May 2012 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: BB-7823 Serial Number: 572 Has Expanded Access? No
Review Board:	Approval Status: Approved Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	This study will evaluate the efficacy and safety of peginterferon alfa-2a 40KD + ribavirin combination therapy given for 24 weeks versus 48 weeks in patients with chronic hepatitis C, genotype 2/3.
Detailed Description:	During a pre-study run-in phase patients with chronic hepatitis C genotype 2/3, who had started therapy with PEG-IFN alfa-2a plus ribavirin according to local standard of care and did not achieve a rapid viral response (RVR) (defined as Hepatitis C virus (HCV) RNA <15 IU/mL at Week 4 of treatment measured with the Roche COBAS AmpliPrep / COBAS TaqMan® HCV Test) were eligible for the study and entered the screening phase between treatment Week 4 and 8 as soon as the result of the Week 4 HCV RNA test was available. Eligible patients entered the study and continued with the dose regimens of PEG-IFN alfa-2a and ribavirin they were taking prior to enrolment into the trial up to Week 24 of treatment. Patients who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24, were randomized at treatment Week 24 to one of the two study groups. Upon randomization, participants either stopped treatment (equaling 24 weeks of treatment) or continued treatment for another 24 weeks (equaling 48 weeks of treatment). A treatment free follow-up period of 24 weeks (for participants in the 48-week treatment group) or 48 weeks (participants in the 24-week treatment group) completed the study.

Conditions

Conditions: Hepatitis C, Chronic

Keywords:

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 3

Intervention Model: Parallel Assignment

Number of Arms: 2

Masking: Open Label

Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 235 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: PEG-IFN alfa-2a + Ribavirin for 24 weeks After 24 weeks of treatment with pegylated interferon alfa-2a (PEG-IFN alfa-2a) 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of hepatitis C virus (HCV) ribonucleic acid (RNA) at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, at which time treatment was stopped. Participants were followed for an additional 48 weeks during the treatment-free follow-up period.	Drug: peginterferon alfa-2a Other Names: • Pegasys® • PEG-IFN alfa-2a Drug: Ribavirin Other Names: • Copegus®
Active Comparator: PEG-IFN alfa-2a + Ribavirin for 48 weeks After 24 weeks of treatment with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, and continued treatment for another 24 weeks (for a total of 48 weeks of	Drug: peginterferon alfa-2a Other Names: • Pegasys® • PEG-IFN alfa-2a Drug: Ribavirin Other Names:

Arms	Assigned Interventions
treatment). Participants were followed for an additional 24 weeks during the treatment-free follow-up period.	• Copegus®

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- adult patients, >=18 years of age;
- serological evidence of chronic hepatitis C (CHC);
- CHC genotype 2 or 3;
- receiving PEGASYS + Copegus according to local standard of care and no rapid viral response (RVR);
- compensated liver disease.

Exclusion Criteria:

- pegylated interferon, standard interferon or ribavirin therapy at any time prior to initiation of current therapy with PEGASYS + Copegus;
- coinfection with hepatitis A or B, or human immunodeficiency virus (HIV);
- history or other evidence of decompensated liver disease.

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Germany
Frankfurt Am Main, Germany, 60590

Berlin, Germany, 13353

Hamburg, Germany, 20099

ULM, Germany, 89081

Heidelberg, Germany, 69120

Köln, Germany, 50937

Tübingen, Germany, 72076

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München, Germany, 81675

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Sao Paulo, Brazil, 04040-003

Sao Paulo, Brazil, 04040-003

Sao Luis, Brazil, 78048-790

Germany

Düsseldorf, Germany, 40225

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Switzerland

Zürich, Switzerland, 8091

Germany

Düsseldorf, Germany, 40237

Kiel, Germany, 24105

Mexico

Puebla, Mexico, 72560

Brazil

Sorocaba, Brazil, 18047-600

Porto Alegre, Brazil, 90020-090

Vitoria, Brazil, 29043-260

Brasilia, Brazil, 70335-000

Belgium
Bruxelles, Belgium, 1000

Antwerpen, Belgium, 2650

Gent, Belgium, 9000

Kortrijk, Belgium, 8500

Liege, Belgium, 4000

Austria
Wien, Austria, 1090

Graz, Austria, 8036

Wien, Austria, 1160

Wien, Austria, 1090

Linz, Austria, 4010

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Albuquerque, New Mexico, United States, 87131

United States, Louisiana
Baton Rouge, Louisiana, United States, 70890

United States, Florida
Jacksonville, Florida, United States, 32256

Orlando, Florida, United States, 32803

United States, Missouri
St Louis, Missouri, United States, 63104

United States, Texas
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San Diego, California, United States, 92103-8465

Long Beach, California, United States, 90822

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Kingsport, Tennessee, United States, 37660

United States, New York
Syracuse, New York, United States, 13210

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Birmingham, Alabama, United States, 35294

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Tupelo, Mississippi, United States, 38801

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Winston-salem, North Carolina, United States, 27103

United States, Georgia
Marietta, Georgia, United States, 30060

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Ribeirao Preto, Brazil, 14049-900

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Fremantle, Australia, 6160

Sydney, Australia, 2139

Darlinghurst, Australia, 2010

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Mexico City, Mexico, 14050

United States, California
Torrance, California, United States, 90505

Los Angeles, California, United States, 90057

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Chapel Hill, North Carolina, United States, 27599-7080

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Sacramento, California, United States, 95816

Los Angeles, California, United States, 90048

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Austria

Oberndorf, Austria, 5110

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Germany
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Offenburg, Germany, 77654

Jena, Germany, 07747

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Vancouver, British Columbia, Canada, V6Z 2K5

Canada, Ontario
Mississauga, Ontario, Canada, L5M 4N4

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Recruitment Details	Patients with Chronic Hepatitis C, Genotype 2 or 3 who had started therapy with PEG-IFN alfa-2a plus ribavirin according to local standard of care during a pre-study run-in phase and did not achieve a rapid viral response defined as HCV RNA <15 IU/mL at Week 4 of treatment were eligible and entered the screening phase between treatment Weeks 4-8.
Pre-Assignment Details	235 patients enrolled and continued with the dose regimens they were taking prior to enrolment up to Week 24 of treatment. Patients who achieved at least a 2-log10 drop of HCV RNA at Week 12 (compared to HCV RNA prior to treatment initiation) or had HCV RNA <15 IU/mL and who were still taking study medication at Week 24, were randomized at Week 24.

Reporting Groups

	Description
PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	After 24 weeks of treatment with pegylated-interferon (peginterferon) alfa-2a (PEG-IFN alfa-2a) 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of hepatitis C virus (HCV) ribonucleic acid (RNA) at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, at which time treatment was stopped. Participants were followed for an additional 48 weeks during the treatment-free follow-up period.
PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	After 24 weeks of treatment with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, and continued treatment for another 24 weeks (for a total of 48 weeks of treatment). Participants were followed for an additional 24 weeks during the treatment-free follow-up period.

Treatment Period

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
Started	95	93
Completed	95 [1]	66 [2]
Not Completed	0	27
Adverse event/intercurrent illness	0	9
Death	0	1
Did not cooperate / refused treatment	0	13
Insufficient therapeutic response	0	2

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
Other	0	1
Withdrawal by Subject	0	1

[1] Patients who completed 24 weeks of treatment
[2] Patients who completed 48 weeks of treatment

Follow-up Period

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
Started	95	93
Completed	66 [1]	78 [2]
Not Completed	29	15
Relapse post-treatment	11	3
Failure to return	10	2
Patient withdrew consent	5	4
HCV-RNA detectable at end of treatment	2	1
Did not cooperate	0	3
Reason not specified	1	1
Death	0	1

[1] Patients who had an HCV RNA sample at 48 weeks of follow-up
[2] Patients who had an HCV RNA sample at 24 weeks of follow-up

Baseline Characteristics

Reporting Groups

	Description
PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	After 24 weeks of treatment with peginterferon alfa-2a (PEG-IFN alfa-2a) 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of hepatitis C virus (HCV) ribonucleic acid (RNA) at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, at which time treatment was stopped. Participants were followed for an additional 48 weeks during the treatment-free follow-up period.

	Description
PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	After 24 weeks of treatment with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, and continued treatment for another 24 weeks (for a total of 48 weeks of treatment). Participants were followed for an additional 24 weeks during the treatment-free follow-up period.

Baseline Measures

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	Total
Number of Participants	95	93	188
Age, Continuous [units: years] Mean (Standard Deviation)	48.8 (9.83)	48.6 (10.12)	48.7 (9.95)
Age, Customized [units: participants]			
≤ 50 years	47	53	100
> 50 years	48	40	88
Gender, Male/Female [units: participants]			
Female	40	39	79
Male	55	54	109
Race/Ethnicity, Customized [units: participants]			
Caucasian or white	82	81	163
Black	8	6	14
Asian or oriental	1	2	3
Other	4	4	8
Hepatitis C virus (HCV) genotype [units: participants]			
HCV Genotype 2	19	19	38
HCV Genotype 3	76	74	150

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	Total
Pre-treatment HCV ribonucleic acid (RNA) [units: log10 IU/mL] Mean (Standard Deviation)	6.11 (0.624)	6.17 (0.773)	6.14 (0.700)
Region [1] [units: participants]			
Non-U.S.	85	82	167
U.S.	10	11	21

[1] Region (US and non-US) was used for stratification.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With a Sustained Virologic Response 24 Weeks After Scheduled Completion of Treatment
Measure Description	Sustained virological response (SVR) is defined as a single last HCV RNA measurement <15 IU/ml (measured using the Roche COBAS AmpliPrep / COBAS TaqMan HCV Test) 24 weeks after scheduled treatment completion, defined as Week 44 or later for participants randomized to the 24-week treatment period or Week 68 or later for participants randomized to the 48-week treatment period. Participants without measurements at the end of the 24-week untreated follow-up period were considered non-responders in the analysis.
Time Frame	24 weeks after scheduled treatment completion (approximately Week 48 for participants in the 24-week treatment group and Week 72 for participants in the 48-week treatment group.
Safety Issue?	No

Analysis Population Description
All randomized patients.

Reporting Groups

	Description
PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	After 24 weeks of treatment with peginterferon alfa-2a (PEG-IFN alfa-2a) 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of hepatitis C virus (HCV) ribonucleic acid (RNA) at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, at which time treatment was stopped. Participants were followed for an additional 48 weeks during the treatment-free follow-up period.

	Description
PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	After 24 weeks of treatment with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, and continued treatment for another 24 weeks (for a total of 48 weeks of treatment). Participants were followed for an additional 24 weeks during the treatment-free follow-up period.

Measured Values

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
Number of Participants Analyzed	95	93
Percentage of Participants With a Sustained Virologic Response 24 Weeks After Scheduled Completion of Treatment [units: percentage of participants]	52	57

Statistical Analysis 1 for Percentage of Participants With a Sustained Virologic Response 24 Weeks After Scheduled Completion of Treatment

Statistical Analysis Overview	Comparison Groups	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks, PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
	Comments	In order to detect an improvement in SVR rate across all strata equivalent to an odds ratio of 2 (i.e. an increase in SVR by 15 to 16 percentage points at a power of 80% and a two-sided significance level of 0.05, 160 patients per treatment group (320 patients in total) were required.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4557
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	Stratified by HCV genotype (2 vs 3), region (US vs non-US) and initial Ribavirin dose (800mg vs 1000-1200mg).

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	0.80
	Confidence Interval	(2-Sided) 95% 0.45 to 1.43

	Estimation Comments	The odds ratio is the ratio of the odds of a response in the 24-week treatment group to the odds of a response in the 48-week treatment group. (second column).

2. Primary Outcome Measure:

Measure Title	Percentage of Participants With a Sustained Virologic Response 24 Weeks After Actual End of Treatment
Measure Description	Sustained virological response (SVR) is defined as a single last HCV RNA measurement <15 IU/ml (measured using the Roche COBAS AmpliPrep / COBAS TaqMan HCV Test) at 24 weeks after actual end of study treatment. For participants in the 48-week treatment group who stopped study treatment prior to Week 48 for any reason, the HCV RNA measurements 24 weeks after actual end of treatment were used in the analysis. Participants without a 24-week post treatment measurement are considered non-responders.
Time Frame	24 weeks after actual end of treatment (range from Week 48 to Week 72).
Safety Issue?	No

Analysis Population Description
All randomized patients.

Reporting Groups

	Description
PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	After 24 weeks of treatment with peginterferon alfa-2a (PEG-IFN alfa-2a) 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of hepatitis C virus (HCV) ribonucleic acid (RNA) at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, at which time treatment was stopped. Participants were followed for an additional 48 weeks during the treatment-free follow-up period.
PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	After 24 weeks of treatment with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, and continued treatment for another 24 weeks (for a total of 48 weeks of treatment). Participants were followed for an additional 24 weeks during the treatment-free follow-up period.

Measured Values

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
Number of Participants Analyzed	95	93
Percentage of Participants With a Sustained Virologic Response 24 Weeks After Actual End of Treatment [units: percentage of participants]	52	61

Statistical Analysis 1 for Percentage of Participants With a Sustained Virologic Response 24 Weeks After Actual End of Treatment

Statistical Analysis Overview	Comparison Groups	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks, PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1934
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	Stratified by HCV genotype (2 vs 3), region (US vs non-US) and initial Ribavirin dose (800mg vs 1000-1200mg).

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	0.68
	Confidence Interval	(2-Sided) 95% 0.38 to 1.21
	Estimation Comments	The odds ratio is the ratio of the odds of a response in the 24-week treatment group to the odds of a response in the 48-week treatment group.

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Virological Response 72 Weeks After Treatment Initiation
Measure Description	Virological response 72 weeks after treatment initiation is defined as the percentage of participants with HCV RNA <15 IU/mL as measured by the Roche COBAS AmpliPrep / COBAS TaqMan® HCV Test at 48 weeks post completion of the 24 week treatment period and 24 weeks post completion of the 48 week treatment period. Participants without Week 72 measurements were considered non-responders in the analysis.
Time Frame	Week 72
Safety Issue?	No

Analysis Population Description

All randomized patients.

Reporting Groups

	Description
PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	After 24 weeks of treatment with peginterferon alfa-2a (PEG-IFN alfa-2a) 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of hepatitis C virus (HCV) ribonucleic acid (RNA) at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, at which time treatment was stopped. Participants were followed for an additional 48 weeks during the treatment-free follow-up period.
PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	After 24 weeks of treatment with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, and continued treatment for another 24 weeks (for a total of 48 weeks of treatment). Participants were followed for an additional 24 weeks during the treatment-free follow-up period.

Measured Values

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
Number of Participants Analyzed	95	93
Percentage of Participants With Virological Response 72 Weeks After Treatment Initiation [units: percentage of participants]	44	57

Statistical Analysis 1 for Percentage of Participants With Virological Response 72 Weeks After Treatment Initiation

Statistical Analysis Overview	Comparison Groups	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks, PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0788
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	Stratified by HCV genotype (2 vs 3), region (US vs non-US) and initial Ribavirin dose (800mg vs 1000-1200mg).

Method of Estimation	Estimation Parameter	Odds Ratio (OR)

Estimated Value	0.59
Confidence Interval	(2-Sided) 95% 0.33 to 1.06
Estimation Comments	The odds ratio is the ratio of the odds of a response in the 24-week treatment group to the odds of a response in the 48-week treatment group.

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Virological Response at End of Treatment
Measure Description	Virological response at the end of treatment was defined as the percentage of participants with HCV RNA <15 IU/mL as measured by the Roche COBAS AmpliPrep / COBAS TaqMan® HCV Test after the last dose of study medication.
Time Frame	End of Treatment (Week 24 and Week 48 for each treatment group respectively).
Safety Issue?	No

Analysis Population Description

All randomized patients. A backward imputation approach was used when the HCV RNA measurement at end of treatment was missing and HCV RNA was <15 IU/mL at the first measurement after the end of treatment time window (the patient was regarded as having virological response at end of treatment).

Reporting Groups

	Description
PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	After 24 weeks of treatment with peginterferon alfa-2a (PEG-IFN alfa-2a) 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of hepatitis C virus (HCV) ribonucleic acid (RNA) at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, at which time treatment was stopped. Participants were followed for an additional 48 weeks during the treatment-free follow-up period.
PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	After 24 weeks of treatment with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, and continued treatment for another 24 weeks (for a total of 48 weeks of treatment). Participants were followed for an additional 24 weeks during the treatment-free follow-up period.

Measured Values

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
Number of Participants Analyzed	95	93
Percentage of Participants With Virological Response at End of Treatment [units: percentage of participants]	93	90

Statistical Analysis 1 for Percentage of Participants With Virological Response at End of Treatment

Statistical Analysis Overview	Comparison Groups	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks, PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5654
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	Stratified by HCV genotype (2 vs 3), region (US vs non-US) and initial Ribavirin dose (800mg vs 1000-1200mg).

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.36
	Confidence Interval	(2-Sided) 95% 0.48 to 3.87
	Estimation Comments	The odds ratio is the ratio of the odds of a response in the 24-week treatment group to the odds of a response in the 48-week treatment group.

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Virological Relapse
Measure Description	Virological relapse defined as the percentage of participants with a virological response at end of treatment but who did not have a sustained virological response 24 weeks after the end of treatment. Virological response at end of treatment is defined as a single last HCV RNA measurement <15 IU/ml measured using the Roche COBAS AmpliPrep / COBAS TaqMan HCV Test at the day of last dose of study medication. Sustained virological response 24 weeks after the actual treatment end (SVR24) is defined as a single last HCV RNA measurement <15 IU/ml at least 20 weeks after treatment end.
Time Frame	End of treatment (Weeks 24 or 48) and 24 weeks after the end of treatment (weeks 48 and 72 in each treatment group respectively).
Safety Issue?	No

Analysis Population Description

Randomized patients with virological response at the end of treatment and at least one post-treatment HCV RNA measurement.

Reporting Groups

	Description
PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	After 24 weeks of treatment with peginterferon alfa-2a (PEG-IFN alfa-2a) 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of hepatitis C virus (HCV) ribonucleic acid (RNA) at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, at which time treatment was stopped. Participants were followed for an additional 48 weeks during the treatment-free follow-up period.
PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	After 24 weeks of treatment with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, and continued treatment for another 24 weeks (for a total of 48 weeks of treatment). Participants were followed for an additional 24 weeks during the treatment-free follow-up period.

Measured Values

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
Number of Participants Analyzed	83	80
Percentage of Participants With Virological Relapse [units: percentage of participants]	41	29

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Sustained Virologic Response 12 Weeks After Actual End of Treatment
Measure Description	Sustained virological response (SVR) is defined as a single last HCV RNA measurement <15 IU/ml (measured using the Roche COBAS AmpliPrep / COBAS TaqMan HCV Test) at 12 weeks after actual end of study treatment. For participants in the 48-week treatment group who stopped study treatment prior to Week 48 for any reason, the HCV RNA measurements 12 weeks after actual end of treatment were used in the analysis. Participants without a 12-week post treatment measurement are considered non-responders.
Time Frame	12 weeks after actual end of treatment (range from Week 36 to Week 60)
Safety Issue?	No

Analysis Population Description

All randomized patients.

Reporting Groups

	Description
PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	After 24 weeks of treatment with peginterferon alfa-2a (PEG-IFN alfa-2a) 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of hepatitis C virus (HCV) ribonucleic acid (RNA) at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, at which time treatment was stopped. Participants were followed for an additional 48 weeks during the treatment-free follow-up period.
PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	After 24 weeks of treatment with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, and continued treatment for another 24 weeks (for a total of 48 weeks of treatment). Participants were followed for an additional 24 weeks during the treatment-free follow-up period.

Measured Values

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
Number of Participants Analyzed	95	93
Percentage of Participants With a Sustained Virologic Response 12 Weeks After Actual End of Treatment [units: percentage of participants]	52	61

Statistical Analysis 1 for Percentage of Participants With a Sustained Virologic Response 12 Weeks After Actual End of Treatment

Statistical Analysis Overview	Comparison Groups	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks, PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1934
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	Stratified by HCV genotype (2 vs 3), region (US vs non-US) and initial Ribavirin dose (800mg vs 1000-1200mg).

Method of Estimation	Estimation Parameter	Odds Ratio (OR)

Estimated Value	0.68
Confidence Interval	(2-Sided) 95% 0.38 to 1.21
Estimation Comments	The odds ratio is the ratio of the odds of a response in the 24-week treatment group to the odds of a response in the 48-week treatment group.

7. Secondary Outcome Measure:

Measure Title	Number of Participants With Adverse Events (AEs)
Measure Description	An AE was defined as a sign or symptom, including intercurrent illness, that occurred during the course of the clinical study after treatment had started. A related AE is an event assessed by the Investigator to be remotely, possibly, or probably related to study treatment according to criteria provided in the protocol. A severe AE was an event graded by the Investigator as "incapacitating with inability to work or perform normal daily activity". A serious AE (SAE) was defined as any experience that suggests a significant hazard, contraindication, side effect or precaution. This includes any experience which was fatal; was life-threatening; required inpatient hospitalization or prolongation of an existing hospitalization; resulted in persistent or significant disability/incapacity; was a congenital anomaly/ birth defect; was medically significant or required intervention to prevent one or other of the outcomes listed above.
Time Frame	From Week 1 through Week 72.
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	After 24 weeks of treatment with peginterferon alfa-2a (PEG-IFN alfa-2a) 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of hepatitis C virus (HCV) ribonucleic acid (RNA) at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, at which time treatment was stopped. Participants were followed for an additional 48 weeks during the treatment-free follow-up period.
PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	After 24 weeks of treatment with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, and continued treatment for another 24 weeks (for a total of 48 weeks of treatment). Participants were followed for an additional 24 weeks during the treatment-free follow-up period.

Measured Values

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
Number of Participants Analyzed	95	93
Number of Participants With Adverse Events (AEs) [units: participants]		
Any AE	81	88
Severe AE	13	24
AE related to PEG-IFN alfa-2a	78	86
AE related to ribavirin	72	83
Serious AE	4	11
SAE related to PEG-IFN alfa-2a	0	7
SAE related to ribavirin	0	4
Deaths	0	1

Reported Adverse Events

Time Frame	72 weeks.
Additional Description	[Not specified]

Reporting Groups

	Description
PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	After 24 weeks of treatment with peginterferon alfa-2a (PEG-IFN alfa-2a) 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of hepatitis C virus (HCV) ribonucleic acid (RNA) at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, at which time treatment was stopped. Participants were followed for an additional 48 weeks during the treatment-free follow-up period.

	Description
PEG-IFN Alfa-2a + Ribavirin for 48 Weeks	After 24 weeks of treatment with PEG-IFN alfa-2a 180 µg/week plus ribavirin 800-1200 mg/day participants who achieved at least a 2-log10 drop of HCV RNA at Week 12 (as compared to HCV RNA levels prior to treatment initiation) or had HCV RNA <15 IU/mL, and who were still taking study medication at treatment Week 24 were randomized into the study, and continued treatment for another 24 weeks (for a total of 48 weeks of treatment). Participants were followed for an additional 24 weeks during the treatment-free follow-up period.

Serious Adverse Events

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
	Affected/At Risk (%)	Affected/At Risk (%)
Total	4/95 (4.21%)	11/93 (11.83%)
Blood and lymphatic system disorders		
Anaemia [A] †	1/95 (1.05%)	1/93 (1.08%)
Thrombocytopenia [A] †	0/95 (0%)	1/93 (1.08%)
Congenital, familial and genetic disorders		
Pyloric stenosis [A] †	1/95 (1.05%)	0/93 (0%)
Gastrointestinal disorders		
Oesophageal varices haemorrhage [A] †	1/95 (1.05%)	0/93 (0%)
Rectal haemorrhage [A] †	0/95 (0%)	1/93 (1.08%)
Vomiting [A] †	0/95 (0%)	1/93 (1.08%)
Infections and infestations		
Cellulitis [A] †	0/95 (0%)	1/93 (1.08%)
Sepsis [A] †	0/95 (0%)	1/93 (1.08%)
Injury, poisoning and procedural complications		
Road traffic accident [A] †	1/95 (1.05%)	0/93 (0%)
Metabolism and nutrition disorders		
Hypertriglyceridaemia [A] †	0/95 (0%)	1/93 (1.08%)
Musculoskeletal and connective tissue disorders		

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
	Affected/At Risk (%)	Affected/At Risk (%)
Intervertebral disc protrusion [A] †	0/95 (0%)	1/93 (1.08%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Colon cancer [A] †	1/95 (1.05%)	0/93 (0%)
Diffuse large B-cell lymphoma [A] †	0/95 (0%)	1/93 (1.08%)
Nervous system disorders		
Cerebrovascular accident [A] †	0/95 (0%)	1/93 (1.08%)
Convulsion [A] †	0/95 (0%)	1/93 (1.08%)
Psychiatric disorders		
Alcohol abuse [A] †	1/95 (1.05%)	0/93 (0%)
Depression [A] †	0/95 (0%)	1/93 (1.08%)
Psychotic disorder [A] †	0/95 (0%)	1/93 (1.08%)
Renal and urinary disorders		
Mesangioproliferative glomerulonephritis [A] †	0/95 (0%)	1/93 (1.08%)
Respiratory, thoracic and mediastinal disorders		
Chronic obstructive pulmonary disease [A] †	0/95 (0%)	1/93 (1.08%)
Skin and subcutaneous tissue disorders		
Skin reaction [A] †	0/95 (0%)	1/93 (1.08%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (15.0)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
	Affected/At Risk (%)	Affected/At Risk (%)
Total	81/95 (85.26%)	87/93 (93.55%)
Blood and lymphatic system disorders		
Anaemia [A] †	8/95 (8.42%)	9/93 (9.68%)
Neutropenia [A] †	7/95 (7.37%)	7/93 (7.53%)
Gastrointestinal disorders		
Abdominal pain [A] †	3/95 (3.16%)	5/93 (5.38%)
Abdominal pain upper [A] †	7/95 (7.37%)	8/93 (8.6%)
Diarrhoea [A] †	7/95 (7.37%)	14/93 (15.05%)
Dry mouth [A] †	2/95 (2.11%)	5/93 (5.38%)
Dyspepsia [A] †	2/95 (2.11%)	10/93 (10.75%)
Nausea [A] †	13/95 (13.68%)	24/93 (25.81%)
Vomiting [A] †	3/95 (3.16%)	5/93 (5.38%)
General disorders		
Asthenia [A] †	18/95 (18.95%)	14/93 (15.05%)
Chills [A] †	1/95 (1.05%)	5/93 (5.38%)
Fatigue [A] †	33/95 (34.74%)	47/93 (50.54%)
Influenza like illness [A] †	14/95 (14.74%)	7/93 (7.53%)
Irritability [A] †	12/95 (12.63%)	4/93 (4.3%)
Pyrexia [A] †	11/95 (11.58%)	11/93 (11.83%)
Investigations		
Weight decreased [A] †	7/95 (7.37%)	9/93 (9.68%)
Metabolism and nutrition disorders		

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
	Affected/At Risk (%)	Affected/At Risk (%)
Decreased appetite [A] †	8/95 (8.42%)	15/93 (16.13%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	10/95 (10.53%)	13/93 (13.98%)
Back pain [A] †	9/95 (9.47%)	3/93 (3.23%)
Myalgia [A] †	8/95 (8.42%)	18/93 (19.35%)
Pain in extremity [A] †	7/95 (7.37%)	6/93 (6.45%)
Nervous system disorders		
Dizziness [A] †	6/95 (6.32%)	9/93 (9.68%)
Headache [A] †	17/95 (17.89%)	30/93 (32.26%)
Psychiatric disorders		
Anxiety [A] †	5/95 (5.26%)	4/93 (4.3%)
Depression [A] †	13/95 (13.68%)	11/93 (11.83%)
Insomnia [A] †	21/95 (22.11%)	21/93 (22.58%)
Sleep disorder [A] †	6/95 (6.32%)	6/93 (6.45%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	7/95 (7.37%)	12/93 (12.9%)
Dyspnoea [A] †	9/95 (9.47%)	9/93 (9.68%)
Dyspnoea exertional [A] †	8/95 (8.42%)	5/93 (5.38%)
Epistaxis [A] †	5/95 (5.26%)	5/93 (5.38%)
Skin and subcutaneous tissue disorders		
Alopecia [A] †	15/95 (15.79%)	17/93 (18.28%)
Dry skin [A] †	13/95 (13.68%)	14/93 (15.05%)
Pruritus [A] †	17/95 (17.89%)	20/93 (21.51%)

	PEG-IFN Alfa-2a + Ribavirin for 24 Weeks	PEG-IFN Alfa-2a + Ribavirin for 48 Weeks
	Affected/At Risk (%)	Affected/At Risk (%)
Rash [A] †	8/95 (8.42%)	9/93 (9.68%)
Vascular disorders		
Hypertension [A] †	2/95 (2.11%)	8/93 (8.6%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (15.0)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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