ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
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Grantor: CDER IND/IDE Number: 58,827 Serial Number: 372

A Study of Induction Dosing With PEGASYS (Peginterferon Alfa-2a [40KD]) Plus Copegus in Treatment-Naive Patients With Chronic Hepatitis C

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by:	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT00394277

Purpose

This 4-arm study will compare the efficacy and safety of PEGASYS induction and maintenance dosing, versus standard fixed dosing in combination with Copegus, and the efficacy and safety of higher dose versus standard dose Copegus in combination with PEGASYS. Patients with chronic hepatitis C (CHC) genotype 1 infection of high viral titer, and baseline body weight ≥85 kg, will be randomized to one of 4 groups, to receive one of the following: a) PEGASYS 180 µg subcutaneously (sc) weekly plus Copegus 1200 mg orally (po) daily; b) PEGASYS 180 µg sc weekly plus Copegus 1400-1600 mg po daily; c)PEGASYS 360 µg sc weekly (induction) followed by 180 µg sc weekly (maintenance) plus Copegus 1200 mg po daily; or d) PEGASYS 360 µg sc weekly (induction) followed by 180 µg sc weekly (maintenance) plus Copegus 1400-1600 mg po daily. Following 48 weeks treatment, there will be a 24-week period of treatment-free follow-up. The anticipated time on study treatment is 3-12 months, and the target sample size is 500+ individuals.

Condition	Intervention	Phase
Hepatitis C, Chronic	Drug: peginterferon alfa-2a Drug: Ribavirin	Phase 4

Study Type: Interventional
Study Design: Treatment, Factorial Assignment, Double Blind (Subject, Investigator), Randomized, Safety/Efficacy Study

Official Title: Randomized, Multicenter, Double-blinded, Phase IV Study Evaluating the Efficacy (as Measured by Sustained Virological Response) and Safety of 360 µg Induction Dosing of Pegasys® in Combination With Higher Copegus® Doses in Treatment-naïve Patients With Chronic Hepatitis C Genotype 1 Virus Infection of High Viral Titer and Baseline Body Weight Greater Than or Equal to 85 kg

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Sustained Virological Response (SVR)-24 (Scheduled Treatment Period) [Time Frame: Week 72] [Designated as safety issue: No]
  SVR-24 according to the scheduled treatment period was defined as the percentage of patients with undetectable HCV RNA at 24 weeks after completion of the treatment period (a single last HCV RNA PCR <15 IU/mL measured at or after week 68 (ie, on or after study day 477).

Secondary Outcome Measures:

- SVR-24 (Actual Treatment Period) [Time Frame: 24 weeks after end of treatment] [Designated as safety issue: No]
  SVR-24 according to the actual treatment period was defined as the percentage of patients with undetectable HCV RNA at least 20 weeks after the last dose of study drug.
- SVR-12 (Scheduled Treatment Period) [Time Frame: 12 weeks after end of treatment] [Designated as safety issue: No]
  SVR-12 according to the scheduled treatment period was defined as the percentage of patients with undetectable HCV RNA at 12 weeks after the scheduled treatment period (a single last HCV RNA PCR <15 IU/mL measured at or after week 60).
- SVR-12 (Actual Treatment Period) [Time Frame: 12 weeks after end of treatment] [Designated as safety issue: No]
  SVR-12 according to the actual treatment period was defined as the percentage of patients with undetectable HCV RNA at least 12 weeks after the last dose of study drug.

Enrollment: 1175
Study Start Date: February 2007
Primary Completion Date: April 2009
Study Completion Date: April 2009

Arms	Assigned Interventions
Experimental: PEG-IFN 180 µg + Ribavirin 1200 mg	Drug: peginterferon alfa-2a 180 µg sc weekly for 48 weeks Other Names: Pegasys Drug: Ribavirin 1200 mg po daily for 48 weeks Other Names: Copegus
Experimental: PEG-IFN 180 µg + Ribavirin 1400/1600 mg	Drug: peginterferon alfa-2a 180 µg sc weekly for 48 weeks Other Names: Pegasys Drug: Ribavirin 1400-1600 mg po daily for 48 weeks

Arms	Assigned Interventions
	Other Names: Copegus
Experimental: PEG-IFN 360/180 µg + Ribavirin 1200 mg	Drug: Ribavirin 1200 mg po daily for 48 weeks Other Names: Copegus Drug: peginterferon alfa-2a 360 µg sc weekly decreasing to 180 µg sc weekly for 48 weeks Other Names: Pegasys
Experimental: PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg	Drug: peginterferon alfa-2a 360 µg sc weekly decreasing to 180 µg sc weekly for 48 weeks Other Names: Pegasys Drug: Ribavirin 1400-1600 mg po daily for 48 weeks Other Names: Copegus

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Adult patients, ≥18 years of age
- CHC infection, genotype 1
- Hepatitis C virus (HCV) RNA ≥400,000 IU/mL
- Baseline body weight ≥85 kg
- Liver biopsy (within 24 months of first dose) with results consistent with CHC

Exclusion Criteria:

- Previous treatment with interferon, ribavirin, viramidine, levovirin, HCV polymerase or protease inhibitors
- Other forms of liver disease, including liver cancer

- Human immunodeficiency virus infection

Contacts and Locations

Locations

United States, Alabama
Birmingham, Alabama, United States, 35294
Huntsville, Alabama, United States, 35801
United States, Alaska
Anchorage, Alaska, United States, 99508
United States, Arizona
Phoenix, Arizona, United States, 85006
United States, California
Fresno, California, United States, 93721
La Jolla, California, United States, 92037-1030
Lancaster, California, United States, 93534
Los Angeles, California, United States, 90095
Los Angeles, California, United States, 90045
Sacramento, California, United States, 95817
San Diego, California, United States, 92105
San Diego, California, United States, 92154
San Diego, California, United States, 92123
San Diego, California, United States, 92103-8465
San Luis Obispo, California, United States, 93401
San Marcos, California, United States, 92069
Ventura, California, United States, 93003
United States, Colorado
Aurora, Colorado, United States, 80045
Englewood, Colorado, United States, 80113
United States, District of Columbia
Washington, District of Columbia, United States, 20010
Washington, District of Columbia, United States, 20037
United States, Florida
Jacksonville, Florida, United States, 32209
Jacksonville, Florida, United States, 32256
Miami, Florida, United States, 33136-1051
North Miami Beach, Florida, United States, 33162
Sarasota, Florida, United States, 34243
United States, Georgia
Atlanta, Georgia, United States, 30308
Austell, Georgia, United States, 30106
Marietta, Georgia, United States, 30060
United States, Hawaii
Honolulu, Hawaii, United States, 96817

United States, Illinois
Chicago, Illinois, United States, 60637
Chicago, Illinois, United States, 60612
Winfield, Illinois, United States, 60190
United States, Indiana
Indianapolis, Indiana, United States, 46202
United States, Iowa
Des Moines, Iowa, United States, 50312
Iowa City, Iowa, United States, 52242-1081
Iowa City, Iowa, United States, 52246
United States, Kentucky
Louisville, Kentucky, United States, 40202
United States, Louisiana
Baton Rouge, Louisiana, United States, 70805
New Orleans, Louisiana, United States, 70112
New Orleans, Louisiana, United States, 70112
United States, Massachusetts
Boston, Massachusetts, United States, 02720
Worcester, Massachusetts, United States, 01068
United States, Michigan
Detroit, Michigan, United States, 48210
Ypsilanti, Michigan, United States, 48197
United States, Minnesota
Plymouth, Minnesota, United States, 55446
United States, Missouri
Kansas City, Missouri, United States, 64131
St Louis, Missouri, United States, 63110
St Louis, Missouri, United States, 63104
United States, New Hampshire
Lebanon, New Hampshire, United States, 03756
United States, New Jersey
Egg Harbour Township, New Jersey, United States, 08234
Vineland, New Jersey, United States, 08360
United States, New York
Bronx, New York, United States, 10467
Manhasset, New York, United States, 11030
New York, New York, United States, 10029
New York, New York, United States, 10021
Rochester, New York, United States, 14618
Williamsville, New York, United States, 14221
Yonkers, New York, United States, 10701
United States, North Carolina
Asheville, North Carolina, United States, 28801
Chapel Hill, North Carolina, United States, 27599-7080
Fayetteville, North Carolina, United States, 28304

United States, Ohio
Cincinnati, Ohio, United States, 45267
Cleveland, Ohio, United States, 44106
Cleveland, Ohio, United States, 44109
United States, Oklahoma
Tulsa, Oklahoma, United States, 74104
United States, Oregon
Medford, Oregon, United States, 97504
United States, Pennsylvania
Lancaster, Pennsylvania, United States, 17604-3200
Philadelphia, Pennsylvania, United States, 19107
Philadelphia, Pennsylvania, United States, 19104
Pittsburgh, Pennsylvania, United States, 15213
United States, Puerto Rico
Ponce, Puerto Rico, United States, 00716
San Juan, Puerto Rico, United States, 00936-5067
Santurce, Puerto Rico, United States, 00909
United States, Rhode Island
Cranston, Rhode Island, United States, 02920
Providence, Rhode Island, United States, 02903
United States, South Carolina
Columbia, South Carolina, United States, 29204
United States, Tennessee
Germantown, Tennessee, United States, 38138
West Nashville, Tennessee, United States, 37205
United States, Texas
Dallas, Texas, United States, 75203
Dallas, Texas, United States, 75390-9034
Dallas, Texas, United States, 75246
Fort Sam Houston, Texas, United States, 78234-3879
Houston, Texas, United States, 77030
Houston, Texas, United States, 77030
United States, Utah
Salt Lake City, Utah, United States, 84121
United States, Virginia
Annandale, Virginia, United States, 22003
Charlottesville, Virginia, United States, 22906-0013
Chesapeake, Virginia, United States, 23320-1706
Fairfax, Virginia, United States, 22031
Richmond, Virginia, United States, 23249
United States, Washington
Seattle, Washington, United States, 98104
Tacoma, Washington, United States, 98405
Vancouver, Washington, United States, 98664
United States, Wyoming

Casper, Wyoming, United States, 82609
Cheyenne, Wyoming, United States, 82001

Belgium
Bruxelles, Belgium, 1200
Bruxelles, Belgium, 1030
Bruxelles, Belgium, 1070
Bruxelles, Belgium, 1000
Gent, Belgium, 9000
Leuven, Belgium, 3000

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Caixa, Brazil, 18618-970
Campinas, Brazil, 13083-888
Juiz de Fora, Brazil, 36036-330
Porto Alegre, Brazil, 90035-003
Porto Alegre, Brazil, 91350-200
Salvador, Brazil, 40110-170
Sao Jose Do Rio Preto, Brazil, 15090-000
Sao Paulo, Brazil, 01307

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Canada, Nova Scotia
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Canada, Ontario
London, Ontario, Canada, N6A 5A5
Ottawa, Ontario, Canada, K1H 8L6
Toronto, Ontario, Canada, M5G 1L7
Toronto, Ontario, Canada, M6H 3M1
Toronto, Ontario, Canada, M5G 1X5

Canada, Quebec
Montreal, Quebec, Canada, H1T 2M4

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Odense, Denmark, 5000

France
Clermont-ferrand, France, 63000
Clichy, France, 92118
Lille, France, 59037
Lyon, France, 69288
Rouen, France, 76031
Strasbourg, France, 67091

Germany

- Berlin, Germany, 13353
- Bonn, Germany, 531105
- Düsseldorf, Germany, 40225
- Frankfurt Am Main, Germany, 60590
- Freiburg, Germany, 79106
- Giessen, Germany, 35392
- Hamburg, Germany, 20246
- Hannover, Germany, 30625
- Heidelberg, Germany, 69120
- Kiel, Germany, 24105
- Köln, Germany, 50924
- Tübingen, Germany, 72076

Hungary

- Bekescsaba, Hungary, 5600
- Budapest, Hungary, 1097
- Budapest, Hungary, 1083
- Debrecen, Hungary, 4032
- Gyor, Hungary, 9024
- Gyula, Hungary, 5700
- Pecs, Hungary, 7654
- Szombathely, Hungary, 9700

Netherlands

- Amsterdam, Netherlands, 1091 AC
- Leiden, Netherlands, 2333 ZA
- Rotterdam, Netherlands, 3015 GD

Poland

- Bydgoszcz, Poland, 85-030
- Chorzow, Poland, 41-500
- Kielce, Poland, 25-317
- Lodz, Poland, 91-347
- Warszawa, Poland, 01-201
- Wroclaw, Poland, 51-124

Romania

- Bucharest, Romania, 022328
- Bucharest, Romania, 010825
- Bucharest, Romania, 021105
- Bucharest, Romania, 030303
- Cluj-napoca, Romania
- Constanta, Romania
- Iasi, Romania, 700111
- Timisoara, Romania

Russian Federation

- Jaloslave, Russian Federation
- Moscow, Russian Federation, 105229
- Moscow, Russian Federation, 143420

Moscow, Russian Federation, 119881
Moscow, Russian Federation, 11/5
Moscow, Russian Federation, 115446
Moscow, Russian Federation, 127009
Moscow, Russian Federation, 117333
Nizhny Novgorod, Russian Federation, 603022
Samara, Russian Federation, 443011
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London, United Kingdom, SE5 9RS
London, United Kingdom, SW17 0QT
Newcastle Upon Tyne, United Kingdom, NE7 7DN
Plymouth, United Kingdom, PL6 8DH
Southampton, United Kingdom, SO16 6YD

Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Clinical Study Report Synopsis

http://www.roche-trials.com/studyResultGet.action?studyResultNumber=NV18210

Responsible Party:	Hoffmann-La Roche (Disclosures Group)
Study ID Numbers:	NV18210
Health Authority:	United States: Food and Drug Administration

Study Results

Participant Flow

Reporting Groups

	Description
PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).

	Description
PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.
PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).
PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.

Overall Study

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
Started	195	196	393	391
Completed	137	136	273	266
Not Completed	58	60	120	125

Baseline Characteristics

Reporting Groups

	Description
PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).
PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.
PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).
PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.

Baseline Measures

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg	Total
Number of Participants	195	196	393	391	1175
Age, Continuous [1] [units: years] Mean (Standard Deviation)	46.1 (9.86)	45.1 (9.50)	45.7 (9.64)	46.0 (10.18)	45.7 (9.83)
Gender, Male/Female [1] [units: Patients]					
Female	37	41	90	73	241
Male	154	148	292	310	904

[1] Intent-to-treat population (all patients treated with at least one dose of either study medication) PEG-IFN 180 µg + Ribavirin 1200 mg: n = 191 PEG-IFN 180 µg + Ribavirin 1400/1600 mg: n = 189 PEG-IFN 360/180 µg + Ribavirin 1200 mg: n = 382 PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg: n = 383

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Sustained Virological Response (SVR)-24 (Scheduled Treatment Period)
Measure Description	SVR-24 according to the scheduled treatment period was defined as the percentage of patients with undetectable HCV RNA at 24 weeks after completion of the treatment period (a single last HCV RNA PCR <15 IU/mL measured at or after week 68 (ie, on or after study day 477).
Time Frame	Week 72
Safety Issue?	No

Analysis Population Description

Intent-to-treat population (all patients treated with at least one dose of either study medication)

Reporting Groups

	Description
PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).

	Description
PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.
PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).
PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.

Measured Values

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
Number of Participants Analyzed	191	189	382	383
Sustained Virological Response (SVR)-24 (Scheduled Treatment Period) [units: Percentage of patients]	37.7	42.9	43.5	40.7

Statistical Analysis 1 for Sustained Virological Response (SVR)-24 (Scheduled Treatment Period)

Statistical Analysis Overview	Comparison Groups	PEG-IFN 180 µg + Ribavirin 1200 mg, PEG-IFN 180 µg + Ribavirin 1400/1600 mg, PEG-IFN 360/180 µg + Ribavirin 1200 mg, PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Comments	This reflects the primary protocol-specified comparison (standard Pegasys induction dosing arms versus pooled Pegasys induction dosing arms). The study was designed to have at least 86% power for testing the null hypothesis of no difference between these two pooled groups, with assumed response rates of 28%, 32%, 36%, and 43% in the four treatment arms.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.584
	Comments	All secondary comparisons were tested at a two-sided significance level of 0.05.
	Method	Cochran-Mantel-Haenszel

	Comments	P-value obtained from CMH test, stratified by country and ribavirin dose strata.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.075
	Confidence Interval	(2-Sided) 95% 0.831 to 1.391
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	SVR-24 (Actual Treatment Period)
Measure Description	SVR-24 according to the actual treatment period was defined as the percentage of patients with undetectable HCV RNA at least 20 weeks after the last dose of study drug.
Time Frame	24 weeks after end of treatment
Safety Issue?	No

Analysis Population Description

Intent-to-treat population (all patients treated with at least one dose of either study medication)

Reporting Groups

	Description
PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).
PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.
PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).
PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.

Measured Values

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
Number of Participants Analyzed	191	189	382	383
SVR-24 (Actual Treatment Period) [units: Percentage of patients]	38.2	43.9	43.5	40.7

Statistical Analysis 1 for SVR-24 (Actual Treatment Period)

Statistical Analysis Overview	Comparison Groups	PEG-IFN 180 µg + Ribavirin 1200 mg, PEG-IFN 180 µg + Ribavirin 1400/1600 mg, PEG-IFN 360/180 µg + Ribavirin 1200 mg, PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Comments	(PEG-IFN 180 µg + Ribavirin 1200 mg and PEG-IFN 180 µg + Ribavirin 1400/1600 mg) vs. (PEG-IFN 360/180 µg + Ribavirin 1200 mg and PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.775
	Comments	All secondary comparisons are tested at a two-sided significance level of 0.05.
	Method	Cochran-Mantel-Haenszel
	Comments	P-value obtained from CMH test, stratified by country and ribavirin dose strata.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.039
	Confidence Interval	(2-Sided) 95% 0.803 to 1.344
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	SVR-12 (Scheduled Treatment Period)
Measure Description	SVR-12 according to the scheduled treatment period was defined as the percentage of patients with undetectable HCV RNA at 12 weeks after the scheduled treatment period (a single last HCV RNA PCR <15 IU/mL measured at or after week 60).

Time Frame	12 weeks after end of treatment
Safety Issue?	No

Analysis Population Description

Intent-to-treat population (all patients treated with at least one dose of either study medication)

Reporting Groups

	Description
PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).
PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.
PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).
PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.

Measured Values

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
Number of Participants Analyzed	191	189	382	383
SVR-12 (Scheduled Treatment Period) [units: Percentage of patients]	40.3	45.0	44.2	41.5

Statistical Analysis 1 for SVR-12 (Scheduled Treatment Period)

Statistical Analysis Overview	Comparison Groups	PEG-IFN 180 µg + Ribavirin 1200 mg, PEG-IFN 180 µg + Ribavirin 1400/1600 mg, PEG-IFN 360/180 µg + Ribavirin 1200 mg, PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Comments	(PEG-IFN 180 µg + Ribavirin 1200 mg and PEG-IFN 180 µg + Ribavirin 1400/1600 mg) vs. (PEG-IFN 360/180 µg + Ribavirin 1200 mg and PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg)

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.973
	Comments	All secondary comparisons are tested at a two-sided significance level of 0.05.
	Method	Cochran-Mantel-Haenszel
	Comments	P-value obtained from CMH test, stratified by country and ribavirin dose strata.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.004
	Confidence Interval	(2-Sided) 95% 0.777 to 1.299
	Estimation Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	SVR-12 (Actual Treatment Period)
Measure Description	SVR-12 according to the actual treatment period was defined as the percentage of patients with undetectable HCV RNA at least 12 weeks after the last dose of study drug.
Time Frame	12 weeks after end of treatment
Safety Issue?	No

Analysis Population Description

Intent-to-treat population (all patients treated with at least one dose of either study medication)

Reporting Groups

	Description
PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).
PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.
PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).

	Description
PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.

Measured Values

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
Number of Participants Analyzed	191	189	382	383
SVR-12 (Actual Treatment Period) [units: Percentage of patients]	40.3	45.5	44.2	42.3

Statistical Analysis 1 for SVR-12 (Actual Treatment Period)

Statistical Analysis Overview	Comparison Groups	PEG-IFN 180 µg + Ribavirin 1200 mg, PEG-IFN 180 µg + Ribavirin 1400/1600 mg, PEG-IFN 360/180 µg + Ribavirin 1200 mg, PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Comments	(PEG-IFN 180 µg + Ribavirin 1200 mg and PEG-IFN 180 µg + Ribavirin 1400/1600 mg) vs. (PEG-IFN 360/180 µg + Ribavirin 1200 mg and PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.951
	Comments	All secondary comparisons are tested at a two-sided significance level of 0.05.
	Method	Cochran-Mantel-Haenszel
	Comments	P-value obtained from CMH test, stratified by country and ribavirin dose strata.
Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.008
	Confidence Interval	(2-Sided) 95% 0.780 to 1.304
	Estimation Comments	[Not specified]

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).
PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.
PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Ribavirin 600 mg administered orally twice daily (total of 1200 mg daily).
PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360 or 180 µg administered subcutaneously once weekly in abdomen or thigh. Patients with a body weight of 85 kg to <95 kg took 600 mg of ribavirin (3 tablets) in the morning and 800 mg (4 tablets) in the evening, or vice versa; total daily dose was 1400 mg. Patients with a body weight ≥ 95 kg took 800 mg of ribavirin (4 tablets) in the morning and evening; total daily dose was 1600 mg.

Serious Adverse Events

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	22/191 (11.52%)	20/189 (10.58%)	36/382 (9.42%)	39/383 (10.18%)
Blood and lymphatic system disorders				
Anaemia	0/191 (0%)	2/189 (1.06%)	2/382 (0.52%)	3/383 (0.78%)
Anaemia Haemolytic Autoimmune	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Pancytopenia	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Thrombocytopenia	2/191 (1.05%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Cardiac disorders				
Acute Coronary Syndrome	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Angina Pectoris	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	2/383 (0.52%)
Arrhythmia	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Atrial Fibrillation	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Cardiac Arrest	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)
Cardiac Failure Congestive	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Myocardial Infarction	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Endocrine disorders				
Hyperthyroidism	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Eye disorders				
Glaucoma	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Retinal Detachment	0/191 (0%)	1/189 (0.53%)	1/382 (0.26%)	0/383 (0%)
Retinal Haemorrhage	1/191 (0.52%)	1/189 (0.53%)	1/382 (0.26%)	0/383 (0%)
Gastrointestinal disorders				
Abdominal Pain	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	2/383 (0.52%)
Intestinal Obstruction	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Pancreatitis Acute	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Small Intestinal Obstruction	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Vomiting	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
General disorders				
Asthenia	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Fatigue	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Gait Disturbance	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Hyperplasia	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Malaise	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Multi-Organ Failure	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)
Non-Cardiac Chest Pain	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pain	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Hepatobiliary disorders				
Cholecystitis	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Cholecystitis Acute	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Cholelithiasis	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	1/383 (0.26%)
Hepatic Failure	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	1/383 (0.26%)
Hepatorenal Syndrome	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)
Infections and infestations				
Abscess Limb	1/191 (0.52%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Anal Abscess	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Appendicitis	0/191 (0%)	0/189 (0%)	3/382 (0.79%)	2/383 (0.52%)
Bronchitis	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)
Bursitis Infective	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Cellulitis	1/191 (0.52%)	0/189 (0%)	2/382 (0.52%)	0/383 (0%)
Gastroenteritis	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	1/383 (0.26%)
Gastroenteritis Viral	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Injection Site Abscess	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Intervertebral Discitis	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Lobar Pneumonia	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Lung Abscess	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Lung Infection	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Osteomyelitis	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Pelvic Abscess	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Pelvic Inflammatory Disease	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Pneumonia	1/191 (0.52%)	3/189 (1.59%)	2/382 (0.52%)	4/383 (1.04%)
Pyelonephritis	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	1/383 (0.26%)

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pyelonephritis Acute	0/191 (0%)	2/189 (1.06%)	0/382 (0%)	0/383 (0%)
Rectal Abscess	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Sepsis	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Subcutaneous Abscess	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)
Injury, poisoning and procedural complications				
Ankle Fracture	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Meniscus Lesion	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Multiple Fractures	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Overdose	0/191 (0%)	1/189 (0.53%)	1/382 (0.26%)	0/383 (0%)
Postoperative Fever	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Radius Fracture	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Venom Poisoning	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Metabolism and nutrition disorders				
Dehydration	0/191 (0%)	0/189 (0%)	2/382 (0.52%)	1/383 (0.26%)
Diabetic Ketoacidosis	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Musculoskeletal and connective tissue disorders				
Back Pain	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Fracture Nonunion	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Intervertebral Disc Protrusion	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Musculoskeletal Chest Pain	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Adenocarcinoma	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Hepatic Neoplasm Malignant	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Pancreatic Carcinoma	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Pancreatic Neoplasm	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Tonsil Cancer	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Nervous system disorders				
Altered State of Consciousness	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)
Cerebral Haemorrhage	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	1/383 (0.26%)
Cerebrovascular Accident	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Headache	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Hepatic Encephalopathy	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)
Metabolic Encephalopathy	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Peripheral Motor Neuropathy	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Syncope	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Transient Ischaemic Attack	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Psychiatric disorders				
Acute Psychosis	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)
Alcoholism	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Bipolar Disorder	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Completed Suicide	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Dependence	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Depression	0/191 (0%)	3/189 (1.59%)	1/382 (0.26%)	0/383 (0%)
Hostility	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Major Depression	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Panic Attack	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	0/383 (0%)
Psychotic Disorder	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)
Suicidal Ideation	0/191 (0%)	0/189 (0%)	2/382 (0.52%)	0/383 (0%)
Suicide Attempt	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)
Renal and urinary disorders				
Calculus Ureteric	0/191 (0%)	0/189 (0%)	2/382 (0.52%)	0/383 (0%)
Renal Failure Acute	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Tubulointerstitial Nephritis	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Respiratory, thoracic and mediastinal disorders				
Alveolitis Fibrosing	1/191 (0.52%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Haemoptysis	0/191 (0%)	0/189 (0%)	0/382 (0%)	2/383 (0.52%)
Pneumothorax	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)
Skin and subcutaneous tissue disorders				
Dermatitis	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Psoriasis	0/191 (0%)	0/189 (0%)	1/382 (0.26%)	0/383 (0%)
Skin Ulcer	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Vascular disorders				
Hypertension	0/191 (0%)	0/189 (0%)	0/382 (0%)	1/383 (0.26%)
Vena Cava Thrombosis	0/191 (0%)	1/189 (0.53%)	0/382 (0%)	0/383 (0%)

Other Adverse Events

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

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	186/191 (97.38%)	179/189 (94.71%)	370/382 (96.86%)	373/383 (97.39%)
Blood and lymphatic system disorders				
Anaemia	23/191 (12.04%)	22/189 (11.64%)	38/382 (9.95%)	54/383 (14.1%)
Neutropenia	9/191 (4.71%)	16/189 (8.47%)	29/382 (7.59%)	28/383 (7.31%)
Gastrointestinal disorders				
Abdominal Pain	6/191 (3.14%)	10/189 (5.29%)	15/382 (3.93%)	13/383 (3.39%)
Abdominal Pain Upper	11/191 (5.76%)	18/189 (9.52%)	28/382 (7.33%)	23/383 (6.01%)
Constipation	5/191 (2.62%)	13/189 (6.88%)	9/382 (2.36%)	14/383 (3.66%)
Diarrhoea	25/191 (13.09%)	27/189 (14.29%)	62/382 (16.23%)	62/383 (16.19%)

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Dry Mouth	5/191 (2.62%)	14/189 (7.41%)	23/382 (6.02%)	23/383 (6.01%)
Dyspepsia	9/191 (4.71%)	12/189 (6.35%)	25/382 (6.54%)	23/383 (6.01%)
Nausea	41/191 (21.47%)	42/189 (22.22%)	112/382 (29.32%)	104/383 (27.15%)
Vomiting	12/191 (6.28%)	19/189 (10.05%)	42/382 (10.99%)	31/383 (8.09%)
General disorders				
Asthenia	28/191 (14.66%)	35/189 (18.52%)	84/382 (21.99%)	80/383 (20.89%)
Chills	42/191 (21.99%)	55/189 (29.1%)	122/382 (31.94%)	132/383 (34.46%)
Fatigue	66/191 (34.55%)	102/189 (53.97%)	184/382 (48.17%)	182/383 (47.52%)
Injection Site Erythema	16/191 (8.38%)	14/189 (7.41%)	28/382 (7.33%)	24/383 (6.27%)
Injection Site Reaction	12/191 (6.28%)	13/189 (6.88%)	20/382 (5.24%)	14/383 (3.66%)
Irritability	34/191 (17.8%)	29/189 (15.34%)	64/382 (16.75%)	66/383 (17.23%)
Malaise	10/191 (5.24%)	10/189 (5.29%)	14/382 (3.66%)	18/383 (4.7%)
Pain	10/191 (5.24%)	18/189 (9.52%)	24/382 (6.28%)	31/383 (8.09%)
Pyrexia	83/191 (43.46%)	78/189 (41.27%)	176/382 (46.07%)	205/383 (53.52%)
Infections and infestations				
Upper Respiratory Tract Infection	11/191 (5.76%)	7/189 (3.7%)	11/382 (2.88%)	16/383 (4.18%)
Investigations				
Weight Decreased	31/191 (16.23%)	31/189 (16.4%)	54/382 (14.14%)	67/383 (17.49%)
Metabolism and nutrition disorders				
Decreased Appetite	30/191 (15.71%)	31/189 (16.4%)	73/382 (19.11%)	85/383 (22.19%)
Musculoskeletal and connective tissue disorders				
Arthralgia	50/191 (26.18%)	49/189 (25.93%)	88/382 (23.04%)	89/383 (23.24%)
Back Pain	21/191 (10.99%)	22/189 (11.64%)	28/382 (7.33%)	23/383 (6.01%)
Muscle Spasms	8/191 (4.19%)	12/189 (6.35%)	13/382 (3.4%)	15/383 (3.92%)
Myalgia	46/191 (24.08%)	44/189 (23.28%)	111/382 (29.06%)	118/383 (30.81%)
Nervous system disorders				

	PEG-IFN 180 µg + Ribavirin 1200 mg	PEG-IFN 180 µg + Ribavirin 1400/1600 mg	PEG-IFN 360/180 µg + Ribavirin 1200 mg	PEG-IFN 360/180 µg + Ribavirin 1400/1600 mg
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Disturbance in Attention	5/191 (2.62%)	6/189 (3.17%)	20/382 (5.24%)	27/383 (7.05%)
Dizziness	14/191 (7.33%)	27/189 (14.29%)	44/382 (11.52%)	59/383 (15.4%)
Headache	75/191 (39.27%)	76/189 (40.21%)	151/382 (39.53%)	168/383 (43.86%)
Psychiatric disorders				
Anxiety	11/191 (5.76%)	18/189 (9.52%)	31/382 (8.12%)	23/383 (6.01%)
Depression	31/191 (16.23%)	33/189 (17.46%)	65/382 (17.02%)	56/383 (14.62%)
Insomnia	46/191 (24.08%)	45/189 (23.81%)	98/382 (25.65%)	113/383 (29.5%)
Respiratory, thoracic and mediastinal disorders				
Cough	27/191 (14.14%)	35/189 (18.52%)	59/382 (15.45%)	69/383 (18.02%)
Dyspnoea	15/191 (7.85%)	15/189 (7.94%)	39/382 (10.21%)	32/383 (8.36%)
Dyspnoea Exertional	6/191 (3.14%)	13/189 (6.88%)	17/382 (4.45%)	16/383 (4.18%)
Epistaxis	10/191 (5.24%)	10/189 (5.29%)	9/382 (2.36%)	14/383 (3.66%)
Oropharyngeal Pain	12/191 (6.28%)	11/189 (5.82%)	16/382 (4.19%)	22/383 (5.74%)
Skin and subcutaneous tissue disorders				
Alopecia	23/191 (12.04%)	20/189 (10.58%)	71/382 (18.59%)	71/383 (18.54%)
Dry Skin	23/191 (12.04%)	22/189 (11.64%)	38/382 (9.95%)	37/383 (9.66%)
Pruritus	34/191 (17.8%)	27/189 (14.29%)	76/382 (19.9%)	59/383 (15.4%)
Rash	38/191 (19.9%)	40/189 (21.16%)	65/382 (17.02%)	78/383 (20.37%)
Vascular disorders				
Hypertension	7/191 (3.66%)	11/189 (5.82%)	16/382 (4.19%)	20/383 (5.22%)

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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