Drug Class Review
on
Pegylated Interferons for
Chronic Hepatitis C Infection

Final Report
Evidence Tables

May 2007

The Agency for Healthcare Research and Quality has not yet seen or approved this report

A literature scan of this topic is done periodically

The purpose of this report is to make available information regarding the comparative effectiveness and safety profiles of different drugs within pharmaceutical classes. Reports are not usage guidelines, nor should they be read as an endorsement of, or recommendation for, any particular drug, use or approach. Oregon Health & Science University does not recommend or endorse any guideline or recommendation developed by users of these reports.

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Note: A scan of the medical literature relating to the topic is done periodically (see http://www.ohsu.edu/ohsuedu/research/policycenter/DERP/about/methods.cfm for scanning process description). Upon review of the last scan, the Drug Effectiveness Review Project governance group elected not to proceed with another full update of this report. Some portions of the report may not be up to date.

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Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	Eligibility	Exclusion
Silva 2006 Argentina, Mexico, Germany COMPARE Efficacy quality: Fair	H2H (early response)		Treatment-naive patients between the ages of 18 and 65 years who were infected with HCV genotype 1a or 1b [with a minimum of 6.0 x 10[5] HCV-RNA IU/mL, determined by quantitative polymerase chain reaction (PCR)]. Additional inclusion criteria were ALT/AST levels =10 times the ULN, normal hemoglobin, white-blood-cell count =4000 cells/lL, neutrophil count =1500 cells/lL, and platelet count =100,000/lL.	Evidence of liver disease due to causes other than chronic HCV infection, HIV positivity, hemoglobinopathy, hemophilia, severe pre-existing psychiatric disease, poorly controlled diabetes mellitus, significant ischemic heart disease, chronic obstructive lung disease, or active autoimmune disease.
Sporea 2006 Romania Efficacy quality: Poor	H2H (early response)		Presence of chronic hepatitis C virus (proven by liver biopsy performed a maximum of 6 months before treatment) and quantification of the viral load (by PCR) before treatment.	Not reported

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	Eligibility	Exclusion
Alfaleh 2004 Saudi Arabia Efficacy quality: Fair	PEG-IFN vs interferon		Persistently raised aminotransferases for at least 6 months; serum antibodies to HCV; HCV RNA found by PCR; and a diagnosis of chronic hepatitis on liver biopsy sample taken in the preceding 12 months.	Age less than 18 or more than 70 years, previous treatment with interferon or ribavirin, neutropenia (fewer than 1500 neutrophils/mm3), thrombocytopenia (fewer than 90,000 platelets/mm3), anemia, serum creatinine more than 1.5 times >ULN, serum alpha-fetoproteins concentration above 25 ng/ml, history of alcohol or hemolytic disease, decompensated cirrhosis, autoimmune hepatitis, hepatitis B infection, HIV infection, current intravenous drug use, severe depressive illness, severe comorbid disease, organ transplant, pregnancy, unwilling to practice contraception, and hepatocellular disease.

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	Eligibility	Exclusion
Bruno 2004 Italy Efficacy quality: Fair	PEG-IFN vs interferon		Previously untreated HCV RNA positive patients aged between 18 to 65 years with ALT values above 1.5 ULN, liver biopsy performed within 6 monhts prior to enrollment and a diagnosis of chronic hepatitis with any degree of fibrosis, hemoglobin >=13g/dl for males, >=12 g/dl for females, WBC cound >3,000/mm3, granulocyte count >1.500/mm3, platelet cound >80,000/,,3, bilirubin, albumin and serum creatinine levels withn normal limits.	Advanced cirrhosis, i.e., large esophageal varices (F2 or more), history of gastrointestinal bleeding, ascites or encephalopathy, hepatocellular carcinoma, anti-HIV or HBsAg positivity. Alcohol abuse (>=80 g/day), parenteral drug addiction if not abtaining for at least 2 years, and any other contraindications to interferon or ribavirin.

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	Eligibility	Exclusion
Derbala 2005 Egypt Efficacy quality: Poor	PEG-IFN vs interferon		Adult patients with chronic active hepatitis C, detectable serum HCV-RNA by RT-PCR, elevated serum ALT activity more than double normal value and histopathological criteria of chronic active hepatitis. Alpha-fetoprotein value within normal range and ultrasound scanning was negative for hepatocellular carcinoma. Female patients had negative serum pregnancy test and were not breastfeeding. Normal serum direct and indirect bilirubin, albumin, and creatinine. Normal thyroid function prior to the study and either non-diabetic or with controlled blood glucose level with HbA1C<8.5%.	Co-infected with HBV, HIV, hemochromatosis, Wilson disease, or other cause for liver disease, neutrophil count <1.5 x 103/ul, platelet count <90 x103/ul or hemoglobin <12 g/dL for female and <13 g/dl for male, positive auto-antibodies including anti-nuclear antibody, anti-mitochondrial antibody, antismooth muscle antibody, patients with history of severe psychiatric disease, seizure disorder, organ transplantation, or severe cardiac or pulmonary disease. Clinically significant retinal abnormalities, clinical gout, substance abuse (alcohol or iv drugs), or showing any medical condition requiring the administration of systemic steroids.

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	Eligibility	Exclusion
Lee 2004 Taiwan Efficacy quality: Fair	PEG-IFN vs interferon		Previously untreated Chinese chronic hepatitis patients with positive serum antibody ot HCV, aged from 18 to 65 years, who had (1) HCV RNA detectable in serum by PCR assay, 2) undergone a liver biopsy within 1 year before entry that was consistent with chronic hepatitis, 3) elevated serum ALT defined as >=2 x ULN for at least two measurements within 6 months preceding the trial entry.	Positive hepatitis B surface antigen, previous liver transplantation, neutropennia (<1500/mm3), thrombocytopenia (<100,000/mm3), anemia (<13 g/dL for males and <12 g/dL for females), HIV infection, decomensated liver disease, other causes of liver disease, abnormal serum creatinine or alfa-fetoprotein level, abnormal thyroid function test, preexisting psychiatric disorders, demoglobinopathies, autoimmune type disease, poorly controlled coexisting medical conditions, or unable to use contraception.
Mangia (A) 2004 Italy Efficacy quality: Fair	PEG-IFN vs interferon		Previously untreated patients aged 18-70 years, with histologically proven chronic hepatitis C; positive for anti-HCV and HCV RNA by PCR and had at least a 1.5-fold increase in ALT levels for at least 6 months before the start of the study. Hemoglobin levles at least 13 g/dL in males and 12 g/dL in females, leukocyte counts at least 3000/mm3 and platelet counts higher than 70,000/mm3.	Contraindications to interferon, ribavirin, and amantadine; immune suppression; concomitant liver disease attributable to a cause other than HCV infection; severe systemic diseases; intravenous drug use; and/or alcohol abuse.

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	Eligibility	Exclusion
Manns 2001 Europe, Canada, Argentina, US Efficacy quality: Fair	PEG-IFN vs interferon		Adults, previously untreated, positive HCV RNA by PCR, recent liver biopsy consistent with chronic hepatitis, elevated ALT.	Decompensated cirrhosis, other causes of liver disease, HIV, organ transplantation, significant other medical or psychiatric conditions, unable to take contraception.

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Study	Trial Type	HIV	Eligibility	Exclusion
Scotto 2005 Efficacy quality: Fair	PEG-IFN vs interferon		HCV-positive chronic hepatitis without previous treatment with IFN-alfa; serum ALT levels at least twice the ULN for at least 6 months before treatment; presence of anti-HCV antibodies determined by means fo a third-generation ELISA and confirmed by additional third generation RIBA; presence of measurable serum HCV RNA; HCV genotype 1b; leukocyte counts >3000/mm3; platelet counts >7500/mm3; hemoglobin concentration >13 g/dl for males and >12 g/dl for females.	Previous episodes of decompensated liver disease (i.e., ascites, bleeding from esophageal varicose veins, encephalopathy), HIV co-infection, active intravenous drug use or a potential cause of liver disease other than HCV.

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Study	Trial Type	HIV	Eligibility	Exclusion
Tsubota 2005 Japan Efficacy quality: Fair	PEG-IFN vs interferon		HCV genotype 1b confirmed by polymerase chain reaction (PCR); serum HCV RNA levels>100,000 international units (IU)/ml on quantitative PCR assay (defined as ‘‘high’’ viral load, Amplicor HCV Monitor Version 2.0, Roche Diagnostics, Tokyo, Japan); serum alanine transaminase (ALT) concentrations above the upper limit of normal (>45 IU/L); a diagnosis of chronic hepatitis on a liver biopsy specimen obtained within the preceding 1 year, using the ranking system for grading of necroinflammation activity and staging of fibrosis; hemoglobin concentration >=12.0 g/dl; neutrophil count >=1,500/ml; platelet count >=100x103/mcl; creatinine clearance >=51 ml/min; body weight between 40 and 100 kg; and age >=20 years.	Liver cancer or severe liver failure, as defined previously; other forms of liver disease; coexisting serious psychiatric or medical illness, including seizure disorders, diabetes mellitus, cardiovascular or lung disease, and autoimmune-type disease; previous organ transplantation; treatment with any other antiviral or immunomodulatory agent administered within the previous 180 days; history of IFN monotherapy or combination therapy with ribavirin; a positive test for hepatitis B surface antigen; hypersensitivity to IFN/PEG-IFN or ribavirin; pregnancy or lactation, including patients’ partners; and if patients were unable to use contraception.

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	Eligibility	Exclusion
Arizcorreta 2004 Spain Efficacy quality: Poor	PEG-IFN vs interferon	HIV subgroup	HIV infection, detected by the presence of anti-HIV antibodies or by indentification of HIV RNA; HCV co-infection, defined as a postivie serological result with a second- or third-generation enzyme-linked immunosorbent assay and the detection of HCV RNA. A maintained increase of serum aminotransferase levels for >=6 months was required. Minimum fibrosis score of >=1.	Clinical or biochemical crieria of decompensated cirrhosis, positive hepatitis B surface antigen, other infectious, autoimmune, tumoral, biliary or vascular-associated liver disease, active alcohol or drug ddependence, a Karnofsky index of <80, absolute neutrophil counts of <1500 cells/ul, a platelet count of <90,000 cells/ul, or a hemoglobin concentration of <11.0g/dL, poorly controlled psychiatric disease, substantial coexisting medical conditions, inability to use contraceptive measures, for any reason, and previous interferon or ribavirin therapy.

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Study	Trial Type	HIV	Eligibility	Exclusion
Carra 2004 France Efficacy quality: Fair	PEG-IFN vs interferon	HIV	Adults who had never received interferon and with the following characteristics: second-generation enzyme-linked immunosorbent ssay positivity for anti-HCV antibodies and polymerase chain reaction-based assay positivity for HCV-RNA in serum; interpretable results of liver biopsy performed within the previous 18 months, showing at least mild activity or fibrosis, anti HIV antibody positivity and a stable plasma HIV-1 RNA level, stable antiretroviral treatment during the preceding 3 months (or no antiretroviral treatment), and a CD4 cell count higher than 200x106/L.	Neutropenia, thrombocytopenia, anemia, serum creatinine level highe4r than 1.70 mg/dL, circulating hepatitis B surface antigen positivity, decompensated cirrhosis (defined as biopsy-proved cirrhosis with serum albumin below the lower limit of normal, a prothrombin level <60%, a total bilirubin level higher than the ULN, or a history of ascites, hepatic encephalopathy or esophageal varices), biliary, tumoral, or vascular liver disease, psychiatric disorders, a history of seizures, cardiovascular disease, poorly controlled diabetes mellitus, or autoimmune disorders, or if they had actively injected illicit drugs 3 months before enrollment or reported daily alcohol intake greater than 40 g (women) or 50 g (men). Women not willing to use effective contraception.

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Study	Trial Type	HIV	Eligibility	Exclusion
Chung 2004 US Adult AIDS Clinical Trials Group A5071 Efficacy quality: Fair	PEG-IFN vs interferon	HIV	HIV-infected subjects 18 years of age or older with a confirmed diagnosis of hepatitis C, as defined by an HCV RNA level of more than 600 IU per milliliter, and had not previously been treated with interferon alfa; a liver biopsy demonstrating abnormal histologic findings consistent with the presence of chronic hepatitis C was required within 48 weeks before study entry. Subjects with cirrhosis were eligible provided they had no evidence of hepatic decompenstion (i.e., ascites, encephalopathy, jaundice, hypoalbuminemia, or coagulopathy).	Clinically significant anemia, neutropenia, or thrombocytopenia, renal disease, positive tests for hepatitis B surface antigen, uncontrolled cardiopulmonary diseaes, poorly controlled psychiatric disease, or an active HIV-related opportunistic infection.

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Study	Trial Type	HIV	Eligibility	Exclusion
Laguno 2004 Spain Efficacy quality: Fair	PEG-IFN vs interferon	HIV subgroup	Previously untreated chronic hepatitis C with HCV RNA positive in plasma, ALT > 1.5fole the ULN and histological modifications in the liver biopsy (fibrosis >1 and/or necroimflammatory activity); control of HIV infection with a viral load <10,000 copies/ml and a CD4 cell count >250 X 106 cells/l, in response to a stable antrretroviral treatment (ART) or without ART if it was not required.	Presence of other causes of hepatopathy, decompensated cirrhosis, pregnancy and potential contraindications for interferon or for ribavirin therapy such as hemoglobinopathies, cardiopathy, autoimmune diseases, major depression or other sevee psychiatric pathologies and active illicit drug consumption within the last 12 months.

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	Eligibility	Exclusion
Poizot-Martin 2003 France Efficacy quality: Poor	PEG-IFN vs interferon	HIV subgroup	Patients who were treated with a dual therapy protocol consisting of at least 6 monhts and up to 12 months of a combination of interferon (peg or not) plus ribavirin.	Not reported.

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Study	Trial Type	HIV	Eligibility	Exclusion
Torriani 2004 Multiple countries APRICOT Efficacy quality: Good	PEG-IFN vs interferon	HIV subgroup	Over age 18, infected with both HIV and HCV, an have anti-HCV antibodies in serum, detactable serum levels of HCV RNA (>600 IU/ml), elevated serum ALT levels documented on 2 or more occasions within the previous 12 months, findings on liver biopsy within the past 15 months that were consistent with the presence of chronic hepatitis C invection, and compensated liver disease (without compromise of lever function or clinically important portal hypertension). Subjects were required either to have been receiving stable antiretroviral therapy for at least six weeks before study entry, with no changes expected for the first eight weeks of the study, or not to have received any antiretroviral therapy for at least eight weeks before randomization and to be able to delay the initiation of antiretroviral therapy for at least six weeks. For the remainder of the study, changes to an existing antiretroviral therapy regimen or initiation of antiretroviral therapy was permitted at the discretion of the investigator.	Active HIV-related opportunistic infection or cancer; an absolute neutrophil count below 1500 per cubic millimeter; a platelet count below 70,000 per cubic millimeter; a hemoglobin level below 11 g per deciliter for women, or below 12 g per deciliter for men; a serum creatinine level more than 1.5 times the upper limit of normal; concurrent infection with hepatitis A or B virus; evidence of decompensated liver disease; severe psychiatric disease, especially depression; clinically significant coexisting medical conditions; and, for women, pregnancy or unwillingness to practice contraception. Participants were also excluded if they had previously received interferon or ribavirin.

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Study	Trial Type	HIV	Eligibility	Exclusion
Fried 2002 Multiple (US, Europe, Australia, Brazil) Pegasys International Study Group Efficacy quality: Fair	PEG-IFN + ribavirin vs PEG-IFN monotherapy		Adults with > 2000 copies of HCV RNA by PCR, elevated ALT levels within 6 mo., liver biopsy consistent with chronic HCV, no previous interferon treatment.	Neutropenia, thrombocytopenia, anemia, HIC, decomensatied liver disease, serum creatinine > 1.5 x normal, poorly controlled psychiatric disease, alcohol or drug dependence within one year, substantial coexisting medical condition.

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Study	Trial Type	HIV	Eligibility	Exclusion
Inati 2005 Lebanon Efficacy quality: Fair	PEG-IFN + ribavirin vs PEG-IFN monotherapy		Transfusion-dependent thalassaemia major patients with chronic HCV infection with at least 2000 copies of HCV RNA/ml of serum by a sensitive polymerase chain reaction (PCR)-based commercial assay . Patients were older than 12 years of age, were infected with genotype 1 or 4 HCV, were treatment naive, and had a liver biopsy consistent with chronic hepatitis C.	Patients were excluded if they had neutropenia, thrombocytopenia, hepatitis B virus or human immunodeficiency virus co-infection, decompensated liver disease, serum creatinine greater than 1.5 times the upper limit of normal, poorly controlled psychiatric disease, or absolute contraindication to either drug.

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Study	Trial Type	HIV	Eligibility	Exclusion
Kamal (A) 2002 Germany Efficacy quality: Poor	PEG-IFN + ribavirin vs PEG-IFN monotherapy		Patients with proven chronic hepatitis C recruited from cohorts participating in 2 trials. Elevated serum ALT value above the upper limit of normal (40 U/L) on 2 occasions during the preceding 6 months, anti–HCV-positive antibody status assessed by second-generation enzyme-linked immunosorbent assay, positive polymerase chain reaction for HCV RNA, lower limit of quantitation of 2000 copies/mL), and had criteria for chronic hepatitis C in the liver biopsy examination performed within the preceding year.	No patients with cirrhosis or bridging fibrosis were enrolled and none had previously been treated with IFN therapy. other liver diseases, such as hepatitis A, hepatitis B, autoimmune hepatitis, alcohol-induced liver disease, drug-induced hepatitis, decompensated liver disease, coinfection with human immunodeficiency virus, neutropenia, thrombocytopenia, creatinine concentration greater than 1.5 times the upper limit of normal, serum alpha-fetoprotein concentration greater than 25 ng/mL, organ transplant, neoplastic disease, severe cardiac or pulmonary disease, unstable thyroid dysfunction, psychiatric disorder, current pregnancy or breast feeding, or therapy with immunomodulatory agents within the past 6 months.

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Study	Trial Type	HIV	Eligibility	Exclusion
Cargnel 2005 Italy Italian Co-infection Study (ICOS) Efficacy quality: Fair	PEG-IFN + ribavirin vs PEG-IFN monotherapy	HIV	HIV-positive patients with compensated, HCV-related chronic liver disease; males or females, 18–65 years of age; baseline CD4+ =300/mm3; HAART in progress for at least 3 months with positive results (HIV-RNA <400 copies/ml); elevated alanine transferase (ALT) and detectable serum HCV-RNA; liver biopsy within 12 months prior to entry to this protocol consistent with chronic hepatitis C – histological grading and staging were scored according to Knodell and Ishak classification; and haemoglobin values =12 g/dl, leukocyte count >3000/mm3 and platelets >100000/mm3.	Previous treatment with IFN, PEG-IFN alone or in combination with RBV; treatment for chronic hepatitis with another antiviral or immunomodulator in the previous 2 years; presence of other causes of liver disease, excluding chronic HCV infection; advanced/decompensated liver disease; presence of serious disease of the central nervous system, cardiovascular system, respiratory tract or retina; haemophilia or other forms of haemoglobinopathy, decompensated diabetes, severe psychiatric disorders, immunomediated diseases or diseases requiring chronic steroid treatment; and drug addiction or alcohol ingestion =80 g/day and/or methadone therapy during the last 2 years.

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Study	Trial Type	HIV	Eligibility	Exclusion
Khalili 2005 US Efficacy quality: Fair	PEG-IFN + ribavirin vs PEG-IFN monotherapy	HIV	Adult patients (=18 years of age) with treatment-naive chronic HCV, plasma HCV RNA >600 IU/mL, and stable HIV infection. Patients had a liver biopsy within 24 months of enrollment consistent with only chronic HCV disease. Compensated cirrhotics (Child-Pugh grade A) were also included. Patients on HAART had to be on stable therapy for at least 6 weeks prior to HCV therapy, with a CD4 cell count of 200/µL or higher or of 100–99/µL plus a plasma HIV RNA level below 5000 copies/mL.	Any chronic liver disease other than HCV, an active HIV-related opportunistic infection and/or malignancy requiring acute systemic therapy, an absolute neutrophil count <750 cells/µL, hemoglobin <10 g/dL in women and <11 g/dL in men, thrombocytopenia (<75,000 platelets/µL), or serum creatinine level >1.5 times the upper limit of normal (ULN). Patients were also excluded if they had a history of severe psychiatric disease, seizure disorder or current anticonvulsant use, an immunologically mediated disease, chronic pulmonary disease, cardiac disease that could be worsened by acute anemia, or poorly controlled thyroid disease.

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
Silva 2006 Argentina, Mexico, Germany COMPARE Efficacy quality: Fair	36	Mean age: 47.0 52.78% male 47.22% female 83.3% white 16.7% Hispanic	100% genotype 1	Treatment naïve	Peginterferon alfa-2b 1.5 µg/kg 1x / week for 8 weeks	13 mg/kg
					Peginterferon alfa-2a 180 µg 1x / week for 8 weeks	13 mg/kg
Sporea 2006 Romania Efficacy quality: Poor	116	Mean age: 50.2 30.17% male 69.83% female	Not reported	69.8% naïve, 21.6% relapsers, 8.6% nonresponders	Peginterferon alfa-2a 180 µg/kg 1x / week for 12 weeks	800-1200 mg
					Peginterferon alfa-2b 1.5 µg/kg 1x / week for 12 weeks	800-1200 mg

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
Alfaleh 2004 Saudi Arabia Efficacy quality: Fair	96	Mean age: 46.8 56.25% male	18.8% genotype 1 81.3% genotypes other than 1, 1a, or 1b	Treatment naïve	peginterferon alfa-2b 100 µg 1x / week for 48 weeks	800 mg
					interferon alfa-2b 3 million units 3x / week for 48 weeks	800 mg

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
Bruno 2004 Italy Efficacy quality: Fair	311	Mean age: 49.7 62.38% male	Not reported	Treatment naïve	peginterferon alfa-2b 1x/week for 48 weeks Weight-based dosing: 100 µg for weight 65 kg or more and 80 µg for weight below 65 kg for the first 8 weeks, followed by a fixed dose of 50 µg once weekly for the next 40 weeks.	1000-1200 mg
					interferon alfa-2b 6 million units every other day for 48 weeks	1000-1200 mg

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
Derbala 2005 Egypt Efficacy quality: Poor	61	Mean age: 40.7 86.89% male	100% genotypes other than 1, 1a, or 1b	Not reported	Peginterferon alfa-2b 1.5 units per kg/body weight 1x / week for 48 weeks	800-1200 mg
					Interferon alfa-2b 3 million units 3x / week for 48 weeks	800-1200 mg

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
Lee 2004 Taiwan Efficacy quality: Fair	153	Mean age: 44.4 68.63% male 100% Asian	0.7% genotype 1a 49.7% genotype 1b 49.6% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alpha-2b 1.5 µg/kg 1x / week for 24 weeks	1000-1200 mg
					Interferon alpha-2b 3 million unit for 24 weeks	1000-1200 mg
Mangia (A) 2004 Italy Efficacy quality: Fair	362	Mean age: 47.6 59.4% male	58.9% genotype 1 41.1% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2a (with amantadine) 180 µg 1x / week for 48 weeks	1000-1200 mg

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
					Interferon alpha-2a (with amantadine) 3 million unit 3x / week for 48 weeks	1000-1200 mg
					Interferon alpha-2a 3 million unit 3x / week for 48 weeks	1000-1200 mg
Manns 2001 Europe, Canada, Argentina, US Efficacy quality: Fair	1530	Mean age: 43.3 (range: 21-68) 65.56% male	68% genotype 1 32.2% genotypes other than 1, 1a, or 1b	Treatment naïve	peginterferon alfa-2b (0.5 µg/kg) 0.5 µg/kg 1x / week for 48 weeks	1000-1200 mg

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
					peginterferon alfa-2b (1.5 µg/kg) 1.5 ug/kg 1x / week for 48 weeks	800 mg
					interferon 2b 1.5 ug/kg 3x / week for 48 weeks	1000-1200 mg
Scotto 2005 Efficacy quality: Fair	78	Mean age: 37.2 46.15% male	100% genotype 1b	Treatment naïve	Peginterferon alfa-2b 1.5 µg/kg 1x / week for 52 weeks	800-1200 mg

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
					Interferon alfa-2b (3x/week) 6 million units 3x / week for 52 weeks	800-1200 mg
					Interferon alfa-2b (daily) 3 million units daily for 52 weeks	800-1200 mg
Tsubota 2005 Japan Efficacy quality: Fair	48	Median age: 53, 55 (range: 20-65) 64.58% male	100% genotype 1b	Treatment naïve	Peginterferon alfa-2b 1.5 µg/kg 1x / week for 48 weeks	600-1000 mg

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
					Interferon alfa-2b 6 million units 3x / week for 48 weeks	600-1000 mg
Arizcorreta 2004 Spain Efficacy quality: Poor	21	Mean age: 34 (range: 33-39) 71.43% male	52.8% genotype 1 0% genotypes other than 1, 1a, or 1b	Not reported	peginterferon alfa-2a 180 µg 1x / week for 48 weeks	800 mg
					interferon 3 million units 3x / week for 48 weeks	800 mg

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
Carra 2004 France Efficacy quality: Fair	412	Mean age: 39.6 73.79% male	48.1% genotype 1 51.4% genotypes other than 1, 1a, or 1b		peginterferon alfa-2b 1.5 µg 1x / week for 48 weeks	800 mg
					interferon alfa-2b 3 million units 3x / week for 48 weeks	800 mg

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
Chung 2004 US Adult AIDS Clinical Trials Group A5071 Efficacy quality: Fair	133	Mean age: 44.5 81.95% male 48% white 33% black 14% Hispanic 5% other	78% genotype 1 22% genotypes other than 1, 1a, or 1b	Treatment naïve	peginterferon alfa-2a 180 µg 1x / week for 48 weeks	600-1000 mg
					interferon alfa-2b 3-6 million units 3x / week for 48 weeks	Ribavirin 600-1000 mg daily

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
Laguno 2004 Spain Efficacy quality: Fair	95	Mean age: 40 68% male	49% genotype 1 51% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2b 100-150 µg (weight-based) 1x / week for 48 weeks	800-1200 mg
					Interferon alpha-2b 3 million units 3x / week for 48 weeks	800-1200 mg

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
Poizot-Martin 2003 France Efficacy quality: Poor	62	Median age: 36 range: 34-40 (interquartile range) 67.74% male	1.6% genotype 1 38.7% genotype 1a 14.5% genotype 1b 45.2% genotypes other than 1, 1a, or 1b	Not reported	Peginterferon alfa-2b 180 µg 1x / week for 6-12 months	Described as "800 mg, two tablets per day" so not clear if 800 or 1600 mg/day.
					Interferon alfa-2b 3 million units 3x / week for 6-12 months	Described as "800 mg, two tablets per day" so not clear if 800 or 1600 mg/day.

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
Torriani 2004 Multiple countries APRICOT Efficacy quality: Good	860	Mean age: 39.9 81.05% male 79% white 10.3% black 0.8% Asian 9.9% other	60.7% genotype 1 39.3% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2a 180 µg 1x / week for 48 weeks	800 mg

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
					Peginterferon alfa-2a (no ribavirin) 180 ug 1x / week for 48 weeks	Placebo
					Interferon alfa-2a 3 million units 3x / week for 48 weeks	800 mg
Fried 2002 Multiple (US, Europe, Australia, Brazil) Pegasys International Study Group Efficacy quality: Fair	1121	Mean age: 42.5 71.36% male 84.1% white 4.7% black 5.7% Asian 5.4% other	32.6% genotype 1a 30.8% genotype 1b 36.6% genotypes other than 1, 1a, or 1b		Peginterferon alfa-2a 180 units 1x / week for 48 weeks	1000-1200 mg

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Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
					Interferon alfa-2b 3 million unit 3x / week for 48 weeks	1000-1200 mg
					Peginterferon alfa-2a (no ribavirin) 180 ug 1x / week for 48 weeks	Placebo
Inati 2005 Lebanon Efficacy quality: Fair	20	Mean age: 19.6 80% male	75% genotype 1 25% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2a (plus placebo) 180 µg 1x / week for 48 weeks	Placebo

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
					Peginterferon alfa-2a (plus ribavirin) 180 µg 1x / week for 48 weeks	10.6 mg/kg
Kamal (A) 2002 Germany Efficacy quality: Poor	42	Mean age: 42.2 59.52% male 40.48% female	16.7% genotype 1a 69% genotype 1b 14.3% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2a 180 µg 1x / week for 48 weeks	800-1200 mg

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
					Peginterferon alfa-2a 180 µg 1x / week for 48 weeks	None
					Interferon alfa-2a 3-6 million units 3x / week for 48 weeks	None
Cargnel 2005 Italy Italian Co-infection Study (ICOS) Efficacy quality: Fair	135	Mean age: 38.5 82.96% male 17.04% female	43.7% genotype 1 56.3% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2b (plus ribavirin) 1.5 µg/kg 1x / week for 48 weeks	800 mg

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	N	Age/ Gender/ Race-Ethnicity	Genotype	Treatment History	Intervention	Ribavirin daily dose
					Peginterferon alfa-2b monotherapy 1.5 µg/kg 1x / week for 48 weeks	None
Khalili 2005 US Efficacy quality: Fair	154	Mean age: 44.4 81.17% male 59% white 27% black 13% other	76% genotype 1 24% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2a (plus ribavirin) 180 mg 1x / week for 48 weeks	800 mg
					Peginterferon alfa-2a (plus placebo) 180 mg 1x / week for 48 weeks	Placebo

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
Silva 2006 Argentina, Mexico, Germany COMPARE Efficacy quality: Fair	ETR: 13/18 (72.22%) Week 8	Measured early viral response only (after 8 weeks of treatment).		
	ETR: 8/18 (44.44%)			
Sporea 2006 Romania Efficacy quality: Poor	ETR: 48/58 (82.76%)	Measured early viral response only (after 12 weeks of treatment). Early viral response: naïve patients: 43/48 (89.6%); p=0.61 vs PEG-IFN alfa-2B relapsers: 4/7 (57.1%); p=0.67 non-responders: 1/3 (33.3%);		
	ETR: 39/58 (67.24%)	Early viral response: naïve patients: 25/33 (75.2%) relapsers: 12/18 (66.6%) non-responders: 2/7 (28.6%)		

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
Alfaleh 2004 Saudi Arabia Efficacy quality: Fair	SVR: 21/48 (43.75%) ETR: 34/48 (70.83%)	Patients with genotype 4 (N=28): Virologic response ETR: 19/28 (67.9%) p=0.42 vs IFN SR: 12/28 (42.9%) p=0.43 vs IFN Biochemical response ETR: 18/28 (64.3%) p=0.79 vs IFN SR: 12/28 (42.9%) p=1.0 vs IFN	ALT: ETR: 34/48 (70.8%) SR: 25/48 (52.1)	
	SVR: 14/48 (29.17%) ETR: 25/48 (52.08%)	Patients with genotype 4 (N=31): Virologic response ETR: 17/31 (54.8%) SR: 10/31 (32.3%) Biochemical response ETR: 18/31 (58.1%) SR: 14/31 (45.2%)	ALT: ETR: 25/48 (70.8%); SR: 21/48 (52.1)	

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
Bruno 2004 Italy Efficacy quality: Fair	SVR: 67/163 (41.1%) ETR: 88/163 (53.99%)	Virologic response ETR by body weight (not reported by group): =70 kg: 85/166 (51.2%) >70 kg: 77/145 (53.1%) p=0.74 SR by body weight: =70 kg: 63/166 (37.9%) >70 kg: 48/145 (33.1%) p=0.37 Biochemical response ETR by body weight (not reported by group): =70 kg: 90/166 (54.2%) >70 kg: 70/145 (48.3%) p=0.29 SR by body weight: =70 kg: 66/166 (39.8%) >70 kg: 49/145 (33.8%) p=0.27	ALT: ETR: 90/163 (55.2%) SR: 68/163 (41.7%)	
	SVR: 44/148 (29.73%) ETR: 61/148 (41.22%)		ALT: ETR: 70/148 (47.3%) SR: 47/148 (31.8%)	

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
Derbala 2005 Egypt Efficacy quality: Poor	SVR: 10/30 (33.33%) ETR: 13/30 (43.33%)		ALT: 56.68 +/- 57.1	
	SVR: 8/31 (25.81%) ETR: 11/31 (35.48%)		ALT: 55.29 +/- 35.4	

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
Lee 2004 Taiwan Efficacy quality: Fair	SVR: 51/76 (67.11%) ETR: 67/76 (88.16%)	Virologic response by genotype ETR, genotype 1: PEG-IFN: 35/38 (92.1%) IFN: 34/39 (87.5%) p=0.254 ETR, genotype non-1: PEG-IFN: 32/38 (84.2%) IFN: 37/38 (97.4%) p=0.079 SR, genotype 1: PEG-IFN: 25/38 (65.8%) IFN: 16/39 (41.0%) p=0.019	ALT: 44/76 (57.9%)	Histologic response at week 48 PEG-IFN (N=41) vs IFN (N=46) Change in total Knodell score: -3.69 (SD 0.46) vs -4.19 (SD 0.43) p=0.431 Change in Knodell necroinflammatory score: -3.04 (SD 0.32) vs -3.40 (SD 0.30) p=0.418 Change in Knodell fibrosis score: -0.55 (SD 0.10) vs -0.88
	SVR: 49/77 (63.64%) ETR: 71/77 (92.21%)		ALT: SR: 47/77 (61.0%)	
Mangia (A) 2004 Italy Efficacy quality: Fair	SVR: 79/121 (65.29%) ETR: 90/121 (74.38%)	SVR by genotype genotype 1 or 4: 37/67 (55.2%) genotype 2 or 3: 42/54 (77.8%) (p vs other treatment groups not reported)	ALT: ETR: 81/121(66.9%) SR: 80 /121 (66.1%)	

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
	SVR: 40/120 (33.33%) ETR: 51/120 (42.5%)	SVR by genotype genotype 1 or 4: 18/79 (22.8%) genotype 2 or 3: 22/41 (53.7%)	ALT: ETR: 51/120 (42.5%) SR: 40 /120 (33.3%)	
	SVR: 54/121 (44.63%) ETR: 59/121 (48.76%)	SVR by genotype genotype 1 or 4: 22/78 (28.2%) genotype 2 or 3: 32/43 (74.4%)	ALT: ETR: 62/121(51.2%) SR: 55 /121 (45.5%)	
Manns 2001 Europe, Canada, Argentina, US Efficacy quality: Fair	SVR: 244/514 (47.47%) ETR: 289/514 (56.23%)	SVR by genotype, p vs IFN + RBV: genotype 1: 118/349 (33.8%), p=0.94 genotype 2 or 3: 122/153 (79.7%), p=0.89 genotype 4, 5, or 6: 4/12 (33%) p>0.99		ETR not reported by genotype Histologic response (Knodell scores): PEG-IFN 1.5 µg/kg (N=339) vs PEG-IFN 0.5 µg/kg (N=361) vs IFN (N=334) Inflammation (mean change): -3.4 vs -3.4 vs -3.4 Inflammation (% with improvement): 68% vs 70% vs 69% Fibrosis (mean change):

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
	SVR: 274/511 (53.62%) ETR: 333/511 (65.17%)	SVR by genotype, p vs IFN + RBV: genotype 1: 145/348 (41.7%), p=0.02 genotype 2 or 3: 121/147 (82.3%), p=0.46		
	SVR: 235/505 (46.53%) ETR: 271/505 (53.66%)	SVR by genotype genotype 1: 114/343 (33.2%) genotype 2 or 3: 115/146 (78.8%) genotype 4, 5, or 6: 6/16 (37.5%)		
Scotto 2005 Efficacy quality: Fair	SVR: 14/26 (53.85%) ETR: 17/26 (65.38%)		ALT: End of treatment: 65.4% Sustained: 50.0%	

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
	SVR: 7/26 (26.92%) ETR: 13/26 (50%)		ALT: End of treatment: 50.0% Sustained: 26.9%	
	SVR: 14/26 (53.85%) ETR: 17/26 (65.38%)		ALT: End of treatment: 57.7% Sustained: 46.1%	
Tsubota 2005 Japan Efficacy quality: Fair	SVR: 12/28 (42.86%) ETR: 17/28 (60.71%)		ALT: ETR: 25/28 (89.3%) SR: 16/28 (57.1%)	

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
	SVR: 8/20 (40%) ETR: 12/20 (60%)		ALT: ETR: 14/20 (70.0%) SR: 11/20 (55.0%)	
Arizcorreta 2004 Spain Efficacy quality: Poor	SVR: 7/11 (63.64%) ETR not reported			
	SVR: 2/10 (20%) ETR not reported			

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
Carra 2004 France Efficacy quality: Fair	SVR: 56/205 (27.32%) ETR: 72/205 (35.12%)	Genotypes 1 or 4: ETR: 32/125 (25.6%); p<0.001 vs interferon SR: 21/125 (16.8%); p=0.006 vs interferon Genotypes 2, 3, or 5: ETR: 40/80 (50.0%); p<=0.87 vs interferon SR: 35/80 (43.8%); p=0.88 vs interferon		Histologic response: Metavir score change was -0.19 in PEG-IFN group vs 0.01 for IFN (p=0.02). Mean change in Ishak grade was -0.57 for PEG-IFN vs -0.26 for IFN (p=0.24). Changes in fibrosis did not differ between groups.
	SVR: 41/205 (20%) ETR: 44/205 (21.46%)	Genotypes 1 or 4: ETR: 8/129 (6.2%) SR: 8/129 (6.2%) Genotypes 2, 3, or 5: ETR: 36/76 (47.5%) SR: 33/76 (43.4%)		

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
Chung 2004 US Adult AIDS Clinical Trials Group A5071 Efficacy quality: Fair	SVR: 18/66 (27.27%) ETR: 27/66 (40.91%)	Genotype 1: ETR: 15/51 (29.4%); p NS vs interferon SR: 7/51 (13.7%); p NS vs interferon Non-genotype 1: ETR: 12/15 (80.0%); NS vs interferon SR: 11/15 (73.3%); p=0.07 vs interferon		Among patients with no virologic response at week 24: 26/37 (70%) patients in PEG-IFN group and 45/57 (79%) in IFN group underwent liver biopsy. Among this group, histologic response was observed in 35% ot patients in PEG-IFN and 36% of those in IFN group. Among patients with a virologic response at week 24, 52% had histologic improvement
	SVR: 8/67 (11.94%) ETR: 8/67 (11.94%)	Genotype 1: ETR: 3/52 (5.8%) SR: 3/52 (5.8%) Non-genotype 1: ETR: 5/15 (33.3%) SR: 5/15 (33.3%)		

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
Laguno 2004 Spain Efficacy quality: Fair	SVR: 23/52 (44.23%) ETR: 27/52 (51.92%)	Virologic response results by genotype: ETR, Genotype 1 or 4: PEG-IFN: 13/32 (41%) IFN: 3/27 (11%) p=0.011 ETR, Genotype 2 or 3: PEG-IFN: 13/19 (68%) IFN: 10/15 (67%) p=0.914 SR, Genotype 1 or 4: PEG-IFN: 12/32 (38%) IFN: 2/27 (7%) p=0.007 ETR, Genotype 2 or 3: PEG-IFN: 10/19 (53%) IFN: 7/15 (47%) p=0.730	ALT: SR: 28/52 (53%)	
	SVR: 9/43 (20.93%) ETR: 13/43 (30.23%)		ALT: SR: 14/43 (33%)	

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
Poizot-Martin 2003 France Efficacy quality: Poor	SVR: 1/20 (5%) ETR: 4/20 (20%)			
	SVR: 8/42 (%) ETR: 13/42 (%)			

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
Torriani 2004 Multiple countries APRICOT Efficacy quality: Good	SVR: 116/289 (40.14%) ETR: 136/289 (47.06%)	Results by genotype ETR: genotype 1: 67/176 (38.1%) genotype 2 or 3: 61/95 (64.2%) SR: genotype 1: 51/176 (30.0%) genotype 2 or 3: 59/95 (62.1%) (all groups NS vs IFN + RBV and vs PEG-IFN + placebo)		

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
	SVR: 58/286 (20.28%) ETR: 90/286 (31.47%)	Results by genotype ETR: genotype 1: 37/175 (21.1%) genotype 2 or 3: 51/90 (56.7%) SR: genotype 1: 24/175 (13.7%) genotype 2 or 3: 32/90 (35.6%)		
	SVR: 33/285 (11.58%) ETR: 40/285 (14.04%)	Results by genotype ETR: genotype 1: 13/171 (7.6%) genotype 2 or 3: 24/89 (30.0%) SR: genotype 1: 12/171 (7.0%) genotype 2 or 3: 18/89 (20.2%)		
Fried 2002 Multiple (US, Europe, Australia, Brazil) Pegasys International Study Group Efficacy quality: Fair	SVR: 254/453 (56.07%) 24 weeks following end of treatment ETR: 313/453 (69.09%)	SVR by genotype, p vs IFN + RBV: genotype 1: 138/298 (46.3%), p=0.01 genotype 2 or 3: 106/140 (75.7%), p=0.005 genotype 4: 10/13 (76.9%), p-value not calculated due to small sample size Body weight of 75 kg or less		

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
	SVR: 195/444 (43.9%) 24 weeks after end of treatment ETR: 197/444 (44.4%)	SVR by genotype gentotype 1: 103/285 (36.1%) gentoype 2 or 3: 88/145 (60.7%) gentoype 4: 4/11 (36.4%)		
	SVR: 65/224 (29%) 24 weeks after end of treatment ETR: 66/224 (29.5%)	SVR by genotype gentotype 1: 30/145 (20.7%) gentoype 2 or 3: 31/69 (44.9%) gentoype 4: 4/9 (44.4%)		
Inati 2005 Lebanon Efficacy quality: Fair	SVR: 4/12 (33.33%) ETR: 5/12 (41.67%)			

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
	SVR: 5/8 (62.5%) ETR: 6/8 (75%)			
Kamal (A) 2002 Germany Efficacy quality: Poor	SVR: 8/14 (57.14%) ETR: 11/14 (78.57%)	Of the 16 patients who achieved a SVR, 10 had genoype 1 (4 in the PEG-IFN monotherapy group, 6 in PEG-IFN + RBV group, none in IFN monothrapy group). All 6 patients with genotype non-1 achieved a SVR (2 in IFN monnotherapy group, 2 in PEG-IFN monotherapy group, and 2 in PEG-IFN + RBV group).		

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
	SVR: 6/14 (42.86%) ETR: 10/14 (71.43%)			
	SVR: 2/14 (14.29%) ETR: 4/14 (28.57%)			
Cargnel 2005 Italy Italian Co-infection Study (ICOS) Efficacy quality: Fair	SVR: 15/69 (21.74%) ETR: 20/69 (28.99%)	PEG-IFN + RBV vs monotherapy Genotype 1-4: ETR: 6/37 (16.2%) vs 5/34 (14.7%); NS SVR: 4/37 (10.8%) vs 3/34 (8.8%); p=0.02 Genotype 2-3: ETR: 14/32 (43.7%) vs 6/32 (18.7%); NS SVR: 11/32 (34.4%) vs 3/32 (9.4%); p=0.02		

Evidence Table 1. Randomized controlled trials of the efficacy of pegylated interferons for chronic hepatitis C infection

Study	Virologic Response (SR=sustained response, ETR= end of treatment response)	Additional Results	Biochemical Response	Histologic Response
	SVR: 6/66 (9.09%) ETR: 11/66 (16.67%)			
Khalili 2005 US Efficacy quality: Fair	SVR: 2/37 (5.41%) ETR: 4/37 (10.81%)			
	SVR: 0/39 (0%) ETR: 1/39 (2.56%)			

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Abergel 2006 France Efficacy quality: Fair	Age between 18 and 75 years, no previous treatment with interferon and/or ribavirin, ALT >ULN at least once during the last 12 months, positive serum HCV-RNA using qualitative PCR and severe fibrosis stage of F3 or F4 at histological examination of the liver.	Recent history of alcohol abuse or IV drug addiction, hemoglobin <12 g/dL in women and <13 g/dL in men, platelets <75,000/µL, neutrophhils <1500/µL, decompensated cirrhosis, albumin <30g/L, prothrombin <60%, bilirubin >34 µmol/L, HCC, chronic hepatitis B infection, and HIV infection.	203	Mean age: 50.2
Berg 2006 Germany Efficacy quality: Fair	Both sexes, aged 18 to 70 years with compensated chronic HCV genotype 1 infection who had not been treated previously with IFN-alfa and/or ribavirin; a positive test for anti-HCV; HCV-RNA level greater than 1000 IU/mL by quantitative reverse-transcription polymerase chain reaction; increased serum ALT levels at screening; a liver biopsy specimen taken in the preceding 18 months of study entry showing chronic hepatitis; neutrophil and platelet counts of at least 1500 µL and 90,000 µL; hemoglobin values of at least 12 g/dL for women and 13 g/dL for men; and creatinine levels less than 1.5 mg/dL.	HCV genotype other than type 1 infection, decompensated liver disease, other causes of liver disease, hepatitis B virus infection, human immunodeficiency virus infection, autoimmune disorders, clinically significant cardiac or cardiovascular abnormalities, organ grafts, systemic infections, clinically significant bleeding disorders, evidence of malignant neoplastic diseases, concomitant immunosuppressive medication, excessive daily intake of alcohol, or drug abuse within the past year. Further exclusion criteria were as follows: unwillingness to use contraception, pregnancy, lactation, and male partners of pregnant women.	455	Mean age: 42.7 (range: 19-70) 54.95% male 45.05% female 95.6% white 1.1% black 2.6% Asian 0.7% other

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Brandao 2006 Brazil Efficacy quality: Fair	Ambulatory interferon-naïve men and women >=18 years old with serologically proven CHC. They should also have quantifiable HCV-RNA (>1000 IU/mL), persistently elevated ALT levels (defined as ALT above the ULN, documented on at least two occasions within the past 6 months), have had a liver biopsy within the past 18 months, which was consistent with CHC without cirrhosis.	None reported.	117	Mean age: 41.6 71.79% male 28.21% female 87.2% white 1.7% black 1.7% Asian 9.4% other

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Buti 2002 Israel and Spain Efficacy quality: Fair	Adult patients with chronic hepatitis C, HCV RNA positive, abnormal alanine transaminase levels, and infected with HCV genotype 1.	Decompensated liver disease, hemoglobin level less than 12 g/dL, human immunodeficiency virus infection, cardiovascular disease, previous treatment with interferon and/or ribavirin, and inability to practice contraception.	55	Mean age: 42.8 60% male 40% female
El-Zayadi 2005 Egypt Efficacy quality: Poor	Detectable HCV-RNA of genotype 4, serum ALT elevated (>1.5 fold), and histologically consistnet with CHC using the Ishak score.	Positive to hepatitis B surface antigen, antihepatitis B core immunoglobulin G antibody, autoimmune or thyroid disorders, leucothrombocyopenia, hemolytic anemia, seizure disorders, decompensated cirrhosis or had either focal lesion on abdominal ultrasonography or elevated alfa-fetoprotein.	180	Mean age: 43.3 95% male 5% female

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Glue 2000 France Efficacy quality: Poor	Adult male and female patients with compensated chronic hepatitis C were determined to be eligible to participate in the study on the basis of being positive for HCV RCA by quantitative polymerase chain reaction assay, having a recent liver biopsy consistent with chronic hepatitis, an abnormal alanine transaminase value at screening or within the previous 6 months, and evidence of compensated liver disease, as manifest by normal prothrombin time, normal albumin, total bilirubin, creatinine and fasting blood sugar, normal hematologic parameters, and normal thyroid-stimulating hormone (TSH). Antibody titers (antinuclear, antismooth muscle, anti-LKM, antimicrosomal, and antithyroid) all had to be less than 1:160. Patients were required to be negative for human immunodeficiency virus and hepatitis B surface antigen, and to have normal a-fetoprotein levels.	Patients were excluded if they had significant other medical or psychiatric illness, substance abuse, or causes for liver disease other than HCV infection. Patients who had participated in clinical trials within 30 days of entering screening, who had received an investigational drug during that period, or who had previous interferon or ribavirin treatment were also excluded.	72	Mean age: 39.8 (range: 20-68) 48.61% male 51.39% female

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Hadziyannis 2004 Efficacy quality: Good	Treatment-naive adult patients with a serum hepatitis C virus RNA concentration greater than 2000 copies/ mL, an elevated serum alanine aminotransferase level documented on 2 or more occasions 14 days or more apart within the previous 6 months, compensated liver disease, and a liver biopsy specimen consistent with chronic hepatitis C obtained in the previous 15 months. Patients with compensated cirrhosis or transition to cirrhosis were classified as Child–Pugh class A.	Neutropenia, thrombocytopenia, anemia, or a medical condition that would be clinically significantly worsened by anemia; serum creatinine level more than 1.5 times the upper limit of normal; co-infection with hepatitis A or B virus or HIV; history of bleeding from esophageal varices or other conditions consistent with decompensated liver disease; organ transplant; severe or poorly controlled psychiatric disease, especially depression; malignant neoplastic disease; severe cardiac or chronic pulmonary disease; immunologically mediated disease (except controlled thyroid disease); seizure disorder; severe retinopathy; alcohol or drug dependence within 1 year of study entry; clinically significant comorbid medical conditions; pregnancy; or unwillingness to practice contraception.	1284	Mean age: 43.4 65.26% male 34.74% female 89.3% white 3% black 6.8% Asian 1.2% other

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Helbling 2006 Switzerland Efficacy quality: Fair	Both genders age 18-70 years, biiopsy proved (within <=12 months) chronic hepatitis C with advanced fibrosis/cirrhosis (Ishak stage F4-F6, as assessed by each participating center's local pathologist), no previous antifiral treatment, elevated ALT on >2 occasions within >=6 months, serum HCV RNA positive , hemoglobin >=11 g/dL, neutrophil count >=1500/µL, platelet count >=75,000/µL, serum creatinine <=1.5 times ULN, normal fasting glucose, Hbs-antigen negative, antinuclear antibodies <=1:160, normal thyroid stimulating hormone, normal alpha-fetoprotein and focal lesions ruled out by ultrasound within 1 month of study entry.	Concomitant liver diseasse, ongoing substance abuse including alcohol (>=80 g/day), hepatocellular carcinoma, clinically relevant disorders of other organs/systems, pregnancy o lactation, refusal to practive effective contraception during treatment/followup, immunomodulatory treatment within 6 months or treatment with any investigational drug within 30 days of study entry.	124	Mean age: 47 (range: 30-68)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Jacobson 2005 US Efficacy quality: Fair	Previously treated CHC patients; virologic nonresponders and relapsers to prior combination therapy with IFN and RBV were required to have been treated for at least 24 wks. Prior response was defined by presence of HCV RNA at completion of the prior course of therapy (nonresponders) or recurrence of viremia in patients who were HCV RNA negative at the end of therapy (relapsers). A liver biopsy showing features consistent with CHC obtained within the previous 36 months, read by a local pathologist, was required. Other inclusion criteria: negative hepatitis B surface antigen, antinuclear antibody titer less than 1:160, anti-smooth muscle antibody titer less than 1:160, no evidence of hemochromatosis, normal alpha-1-antitrypsin, and no known human immunodeficiency virus infection. There were no serum ALT criteria for inclusion. Thus, patients with normal ALT levels were allowed entry to the study.	Patients with histologic evaluations using scoring systems other thanMETAVIRwere not included in the analyses based on histology. Patients with concomitant liver diseases were excluded.	321	74.45% male 25.55% female 70% white 16% black 15% other

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Kamal (B) 2005 Egypt Efficacy quality: Fair	Adult males and females with documented chronic hepatitis C according to the following criteria: elevated serum ALT above the upper limit of normal (40 U/l) on two occasions during the preceding six months; anti-HCV positive antibody status assessed by second generation enzyme linked immunosorbent assay positive polymerase chain reaction for HCV RNA; genotype 4; and criteria for chronic hepatitis C in liver biopsy performed within the preceding year with no signs of cirrhosis or bridging fibrosis on pretreatment liver biopsy.	Previous IFN-alfa therapy; other liver diseases such as hepatitis A, hepatitis B, schistosomiasis, autoimmune hepatitis, alcoholic liver disease, drug induced hepatitis, or decompensated liver disease; coinfection with schistosomiasis or human immunodeficiency virus; neutropenia; thrombocytopenia; creatinine concentration >1.5 times the upper limit of normal; serum alfa fetoprotein concentration >25 ng/ml; organ transplant; neoplastic disease; severe cardiac or pulmonary disease; unstable thyroid dysfunction; psychiatric disorder; current pregnancy or breast feeding; or therapy with immunomodulatory agents within the last six months.	287	Mean age: 42.2 52.26% male 47.74% female

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Lodato 2005 Italy Efficacy quality: Fair	Detectable HCV-RNA by PCR elevated (>1.5x) serum ALT for at least 6 months, evidence of compensated liver disease shown by normal values of albumin, prothrombin time, creatinine, bilirubin, hematological parameters (including platelets >150,000 mm3) and fasting blood sugar. Patients who received one single course of interferon monotherapy were allowed to enter the study.	HIV positivity, elevated levels of thyroid stimulating hormone, positivity of auto-antibodies, HBxAg positivity, significant history of cardiovascular and psychiatric disease, and previous combination therapy.	65	Mean age: 49.3 53.85% male 46.15% female

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Mangia (B) 2005 Italy Efficacy quality: Fair	Patients with HCV genotype 2 or 3; 18 to 70 years of age; had antibodies to HCV, infection with genotype 2 or 3, and abnormal alanine aminotransferase levels; and had not received therapy.	Leukocyte count lower than 3000 per cubic millimeter, a platelet count lower than 80,000 per cubic millimeter, a hemoglobin level lower than 12 g per deciliter for women and lower than 13 g per deciliter for men, infection with the human immunodeficiency virus, alcohol intake greater than 20 g daily, and the presence of drug abuse, chronic disease, psychiatric disease, autoimmune disease, or pregnancy and lactation.	283	Mean age: 47.4 55.83% male 44.17% female
Mathew 2006 US Efficacy quality: Poor	Patients enrolled into a randomized study for re-treatment of HCV refractory to prior therapy with interferon alfa-2b in combination with ribavirin. Chronic hepatitis C documented by a positive HCV RNA, abnormal liver tests and liver biopsy consistent with HCV. Minimum hematological criteria included hemoglobin >10 gm/dl for females and 11 for males, WBC counts >3000/ml and platelet count >70000/ml.	Patients with hepatitis B or HIV coinfection, neoplastic disease, severe cardiac or pulmonary disease and psychiatric disorders.	152	Mean age: 46 (range: 28-69) 73.68% male 26.32% female 90% white 5.9% black 2.6% Asian 2% Hispanic

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Meyer-Wyss 2006 Switzerland Efficacy quality: Poor	Treatment-naïve patients (both genders, aged 18-65 years) with biopsy-proven (within <=12 months) chronic hepatis C and up to moderate fibrosis (Metavir score <=F2, as judged by the local hepatopathologist in each participating center), with elevated ALT on at least 2 occasions, at least 6 months apart, and HCV-RNA-positive serum.	Participation in any study within 30 days prior to entry into the trial, pregnant or nursing women, positive HIV status, any liver disease other than chronic hepatitis C, elvated levles of fasting blood glucose, abnormal values of thyroid stimulating hormone, hemophilia or hemoglobinopathy, and any known pre-existing medical condition that could interfere with the patient's participation and completion of the study. This included a history of severe psychiatric disorders, central nervous system trauma or active seizure disorders, significant cardiovascular, pulmonary, or retinal disorders, clinically manifested gout, substance abuse, chronic systemic administration of steroids or other immunosuppressants, or immunologically mediated disease.	219	Mean age: 40.4 63.93% male 36.07% female

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Sanchez-Tapias 2006 Spain Efficacy quality: Fair	Older than 18 years, persistent increase of serum alanine transaminase levels during the past 6 months, positive anti-HCV antibody test, serum HCV-RNA concentration greater than 600 IU/mL, histologic evidence of chronic hepatitis in a liver biopsy specimen obtained within the preceding 24 months, and provision of written informed consent to participate in the study.	Decompensated liver disease; co-existing serious medical or psychiatric illness; liver disease other than that caused by HCV infection; neutrophil count less than 1.5 x 10<9>/L; platelet count less than 90 x 10<9>/L; hemoglobin concentration less than 12 g/dL in women or less than 13 g/dL in men; serum creatinine level greater than 1.5 times the upper limit of the normal range; and presence of co-infection with hepatitis A virus, hepatitis B virus, or the human immunodeficiency virus. Patients also were excluded if they had received any systemic antiviral, antineoplastic, or immunomodulatory therapy within 6 months before the study. Pregnant and breast-feeding women and male partners of pregnant women also were excluded.	326	Mean age: 43.0 65.95% male 34.05% female

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Von Wagner 2005 Germany Efficacy quality: Fair	Male and female patients above 18 years of age with compensated chronic HCV infection not previously treated with interferon-alfa and/or ribavirin, who tested positive for anti-HCV antibody and for HCV RNA, had a liver biopsy specimen taken within 18 months prior to the screening visit showing chronic hepatitis and had at least 1 serum ALT level elevated at screening or entry into the trial. Entry neutrophil and platelet counts had to be at least 1500/µL and 90,000/µL, respectively. Hemoglobin values at entry visit had to be at least 12 g/dL for females and at least 13 g/dL for males.	Any other cause of liver disease or other relevant disorders including human immunodeficiency or hepatitis B virus coinfection; clinically significant hematologic, hepatic, metabolic, renal, rheumatologic, neurologic, or psychiatric disease; clinically significant cardiac or cardiovascular abnormalities; organ grafts; systemic infection; clinically significant bleeding disorders; evidence of malignant neoplastic disease; concomitant immunosuppressive medication; excessive daily intake of alcohol; or drug abuse within the past year. Further exclusion criteria were pregnancy and lactation and male partners of pregnant women.	153	Mean age: 38.8 63.4% male 36.6% female

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Eligibility	Exclusion	N	Age/Gender/Race-Ethnicity
Yu 2006 Taiwan Efficacy quality: Fair	Previously untreated Taiwanese chronic hepatitis C patients, aged from 18 to 65 years old, who: (1) were seropositive for HCV antibodies and HCV RNA by polymerase chain reaction; (2) had undergone a liver biopsy within 1 year before entry that was consistent with chronic hepatitis; (3) had displayed elevated serum ALT, defined as >= 1.5 times the upper limit of the normal range for at least two measurements within 6 months preceding the trial entry; and (4) possessed an HCV genotype 1b infection.	Patients with HCV genotype other than 1b infection, hepatitis B surface antigen, HIV infection, autoimmune hepatitis, primary biliary cirrhosis, sclerosing cholangitis, Wilson's disease, a1-antitrypsin deficiency, decompensated cirrhosis (Child–Pugh class B or C), overt hepatic failure, a current or past history of alcohol abuse (>= 80 ml ethanol/ day), psychiatric condition, previous liver transplantation or with evidence of hepatocellular carcinoma were excluded.	60	Mean age: 45.3 65% male 35% female

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
Abergel 2006 France Efficacy quality: Fair	51.2% genotype 1 48.8% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2b (1.5 µg/kg) 1.5 µg/kg 1x / week for 48 weeks	800 mg daily	SVR: 45/101 (44.55%) ETR: 59/101 (58.42%)
			Peginterferon alfa-2b (0.75 µg/kg) 0.75 µg/kg 1x / week for 48 weeks	800 mg daily	SVR: 38/102 (37.25%) ETR: 57/102 (55.88%)
Berg 2006 Germany Efficacy quality: Fair	28% genotype 1a 63.2% genotype 1b 9% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2a (48 weeks) 180 µg 1x / week for 48 weeks	800 mg daily	SVR: 121/230 (52.61%) ETR: 163/230 (70.87%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
			Peginterferon alfa-2a (72 weeks) 180 µg 1x / week for 72 weeks	800 mg daily	SVR: 121/225 (53.78%) ETR: 142/225 (63.11%)
Brandao 2006 Brazil Efficacy quality: Fair	53.8% genotype 1 46.1% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2a (genotype 1, 24 weeks) 180 µg 1x / week for 24 weeks	800 mg daily	SVR: 9/32 (28.12%) ETR: 17/32 (53.12%)
			Peginterferon alfa-2a (genotype 1, 48 weeks) 180 µg 1x / week for 48 weeks	800 mg daily	SVR: 15/31 (48.39%) ETR: 24/31 (77.42%)
			Peginterferon alfa-2a (genotype non-1, 24 weeks) 180 µg 1x / week for 24 weeks	800 mg daily	SVR: 41/54 (75.93%) ETR: 47/54 (87.04%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
Buti 2002 Israel and Spain Efficacy quality: Fair	100% genotype 1	Treatment naïve	Peginterferon alfa-2b (high dose) 1.0 µg/kg 1x / week for 48 weeks	800 mg daily	
			Peginterferon alfa-2b (low dose) 0.5 µg/kg 1x / week for 48 weeks	800 mg daily	
El-Zayadi 2005 Egypt Efficacy quality: Poor	100% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2b (48 weeks) 100 µg 1x / week for 48 weeks	1000-1200 mg daily	SVR: 22/40 (55%) ETR: 26/40 (65%)
			Peginterferon alpha-2b (24 weeks) 100 ug 1x / week for 24 weeks	1000-1200 mg daily	SVR: 34/70 (48.57%) 0.014 vs IFN + RBV for 24 weeks ETR: 46/70 (65.71%)
			Interferon alpha-2b 3 million unit daily for 24 weeks	1000-1200 mg daily-1x/week	SVR: 20/70 (28.57%) 0.014 vs Peg-IFN + RBV for 24 weeks ETR: 33/70 (47.14%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
Glue 2000 France Efficacy quality: Poor	0% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2b (0.35 + RBV) 0.35 µg/kg 1x / week for 24 weeks	800-1200 mg daily	SVR: 2/12 (16.67%) ETR: 7/12 (58.33%)
			Peginterferon alfa-2b (0.35 alone) 0.35 µg/kg 1x / week for 24 weeks		SVR: 0/6 (0%) ETR: 3/6 (50%)
			Peginterferon alfa-2b (0.7 + RBV) 0.7 µg/kg 1x / week for 24 weeks	800-1200 mg daily	SVR: 8/15 (53.33%) ETR: 11/16 (68.75%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
			Peginterferon alfa-2b (0.7 alone)		SVR: 4/9 (44.44%) ETR: 5/8 (62.5%)
			Peginterferon alfa-2b (1.4 + RBV)		SVR: 9/15 (60%) ETR: 13/16 (81.25%)
			Peginterferon alfa-2b (1.4 alone)		SVR: 3/7 (42.86%) ETR: 4/8 (50%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
Hadziyannis 2004 Efficacy quality: Good	57.6% genotype 1 80.7% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2a (24 weeks, low dose RBV) 180 µg 1x / week for 24 weeks	800 mg daily	SVR: 110/197 (55.84%) ETR: 159/197 (80.71%)
			Peginterferon alfa-2a (24 weeks, standard RBV) 180 µg 1x / week for 24 weeks	1000-1200 mg daily	SVR: 167/262 (63.74%) ETR: 222/262 (84.73%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
			Peginterferon alfa-2a (48 weeks, low dose RBV) 180 µg 1x / week for 48 weeks	800 mg daily	SVR: 181/349 (51.86%) ETR: 231/349 (66.19%)
			Peginterferon alfa-2a (48 weeks, standard RBV) 180 µg 1x / week for 48 weeks	1000-1200 mg daily	SVR: 263/424 (62.03%) ETR: 317/424 (74.76%)
Helbling 2006 Switzerland Efficacy quality: Fair	44.4% genotype 1 54% genotypes other than 1, 1a, or 1b	Not reported	Peginterferon alfa-2a (standard RBV) 180 µg 1x / week for 48 weeks	1000-1200 mg daily	SVR: 33/64 (51.56%) ETR not reported

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
			Peginterferon alfa-2a (low RBV) 180 µg 1x / week for 48 weeks	600-800 mg daily	SVR: 23/60 (38.33%)
Jacobson 2005 US Efficacy quality: Fair	89% genotype 1 11% genotypes other than 1, 1a, or 1b	See comment	Peginterferon alfa-2b (higher dose) 1.5 µg/kg 1x / week for 48 weeks	800 mg daily	SVR: 29/160 (18.12%) ETR: 60/160 (37.5%)
			Peginterferon alfa-2b (lower dose) 1.0 µg/kg 1x / week for 48 weeks	1000-1200 mg daily	SVR: 21/161 (13.04%) ETR: 37/161 (22.98%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
Kamal (B) 2005 Egypt Efficacy quality: Fair	100% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2b (24 weeks) 1.5 µg/kg 1x / week for 24 weeks	10.6 mg/kg daily	SVR: 28/95 (29.47%) ETR: 45/95 (47.37%)
			Peginterferon alfa-2b (24 weeks) 1.5 µg/kg 1x / week for 24 weeks	10.6 mg/kg daily	SVR: 28/95 (29.47%) ETR: 45/95 (47.37%)
			Peginterferon alfa-2b (36 weeks) 1.5 µg/kg 1x / week for 36 weeks	10.6 mg/kg daily	SVR: 63/96 (65.62%) ETR: 65/96 (67.71%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
			Peginterferon alfa-2b (36 weeks) 1.5 µg/kg 1x / week for 36 weeks	10.6 mg/kg daily	SVR: 63/96 (65.62%) ETR: 65/96 (67.71%)
			Peginterferon alfa-2b (48 weeks) 1.5 µg/kg 1x / week for 48 weeks	10.6 mg/kg daily	SVR: 66/96 (68.75%) ETR: 67/96 (69.79%)
			Peginterferon alfa-2b (48 weeks) 1.5 µg/kg 1x / week for 48 weeks	10.6 mg/kg daily	SVR: 66/96 (68.75%) ETR: 67/96 (69.79%)
Lodato 2005 Italy Efficacy quality: Fair	100% genotypes other than 1, 1a, or 1b	40% naïve, 33.8% non-responders, 26.2% relapsers	Peginterferon alfa-2b (1x/week) 1.5 µg/kg 1x / week for 24-48 weeks	10.6 mg/kg daily	SVR: 8/22 (36.36%) ETR: 11/22 (50%)
			Peginterferon alfa-2b (2x/week) 1.5 µg/kg 2x / week for 24-48 weeks	10.6 mg/kg daily	SVR: 26/43 (60.47%) ETR: 29/43 (67.44%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
Mangia (B) 2005 Italy Efficacy quality: Fair	100% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2b (standard duration) 1.0 µg/kg 1x / week for 24 weeks	1000-1200 mg daily	SVR: 53/70 (75.71%) ETR: 55/70 (78.57%)
			Peginterferon alfa-2b (variable duration) 1.0 µg/kg 1x / week for 12 or 24 weeks	1000-1200 mg daily	SVR: 164/213 (77%) ETR: 180/213 (84.51%)
Mathew 2006 US Efficacy quality: Poor	8.4% genotype 1 16.4% genotypes other than 1, 1a, or 1b	63% nonresponder, 30% relapser, 7% unavailable	Peginterferon alfa-2b (high dose) 1.5 µg/kg 1x / week for 48 weeks	1000-1200 mg daily	SVR: 15/72 (20.83%) Not reported
			Peginterferon alfa-2b (low dose) 0.5 µg/kg 1x / week for 48 weeks	1000-1200 mg daily	SVR: 10/80 (12.5%) Not reported

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
Meyer-Wyss 2006 Switzerland Efficacy quality: Poor	51.6% genotype 1 48.4% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2b (1.0 µg/kg) 1.0 µg/kg 1x / week for 24-48 weeks	800 mg daily	SVR: 61/115 (53.04%) NR
			Peginterferon alfa-2b (1.5 µg/kg) 1.5 µg/kg 1x / week for 24-48 weeks	800 mg daily	SVR: 56/112 (50%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
Sanchez-Tapias 2006 Spain Efficacy quality: Fair	89.3% genotype 1 10.7% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2a (48 weeks) 180 µg 1x / week for 48 weeks	800 mg daily	SVR: 53/165 (32.12%) ETR: 101/165 (61.21%)
			Peginterferon alfa-2a (72 weeks) 180 µg 1x / week for 72 weeks	800 mg daily	SVR: 73/161 (45.34%) ETR: 99/161 (61.49%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
Von Wagner 2005 Germany Efficacy quality: Fair	100.1% genotypes other than 1, 1a, or 1b	Treatment naïve	Peginterferon alfa-2a (16 weeks) 180 µg 1x / week for 16 weeks	800-1200 mg daily	SVR: 58/71 (81.69%) ETR: 67/71 (94.37%)
			Peginterferon alfa-2a (24 weeks) 180 µg 1x / week for 24 weeks	800-1200 mg daily	SVR: 57/71 (80.28%) ETR: 60/71 (84.51%)

Evidence Table 2. Dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	Genotype	Treatment History	Intervention	Ribavirin daily dose	Virologic Response (SVR=sustained virologic response, ETR=end of treatment response)
Yu 2006 Taiwan Efficacy quality: Fair	100% genotype 1b	Treatment naïve	Peginterferon alfa-2b (24 weeks) 80-100 µg 1x / week for 24 weeks	1000-1200 mg daily	SVR: 22/45 (48.89%) ETR: 39/45 (%)
			Peginterferon alfa-2b (48 weeks) 80-100 µg 1x / week for 48 weeks	1000-1200 mg daily	SVR: 12/15 (80%) ETR: 14/15 (93.33%)

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Abergel 2006 France	PEG-IFN at different doses/duration	Fair	Method not described	Yes	Yes	Yes
Alfaleh 2004 Saudi Arabia	PEG-IFN vs interferon	Fair	Yes	Yes	Yes	Yes
Arizcorreta 2004 Spain	PEG-IFN vs interferon	Poor	Method not described	Method not described	No HCV viral load 1.02 vs. 5.56 x 10^6	Yes
Berg 2006 Germany	PEG-IFN at different doses/duration	Fair	Method not described	Yes	Yes	Yes
Brandao 2006 Brazil	PEG-IFN at different doses/duration	Fair	Method not described	Yes	Yes	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Bruno 2004 Italy	PEG-IFN vs interferon	Fair	Yes	Method not described	Yes	Yes
Buti 2002 Israel and Spain	PEG-IFN at different doses/duration	Fair	Method not described	Method not described	No	Yes
Cargnel 2005 Italy Italian Co-infection Study (ICOS)	PEG-IFN + ribavirin vs PEG-IFN monotherapy	Fair	Method not described	Method not described	Yes	Yes
Carrat 2004 France	PEG-IFN vs interferon	Fair	Yes	Yes	Yes	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Chung 2004 US Adult AIDS Clinical Trials Group A5071	PEG-IFN vs interferon	Fair	Method not described	Method not described	Yes	Yes
Crespo 2007 Spain	PEG-IFN vs interferon	Fair	Method not described	Method not described	Yes	Yes
Derbala 2005 Egypt	PEG-IFN vs interferon	Poor	Method not described	Method not described	Unable to determine Baseline characteristics reported for 61 of 70 patients randomized	Yes
El-Zayadi 2005 Egypt	PEG-IFN at different doses/duration	Poor	Not randomized	Not randomized	Yes	Yes
Fried 2002 Multiple (US, Europe, Australia, Brazil) Pegasys International Study Group	PEG-IFN + ribavirin vs PEG-IFN monotherapy	Fair	Method not described	Method not described	Yes	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Glue 2000 France	PEG-IFN at different doses/duration	Poor	Method not described	Method not described	NR	Yes
Hadziyannis 2004	PEG-IFN at different doses/duration	Good	Yes	Yes	No Designed for unequal allocation of HCV genotype 1 and baseline titer	Yes
Helbling 2006 Switzerland	PEG-IFN at different doses/duration (RBV dose)	Fair	Yes	Yes	Yes	Yes
Inati 2005 Lebanon	PEG-IFN + ribavirin vs PEG-IFN monotherapy	Fair	Yes	Method not described	Yes Ferritin level lower in monotherapy group (1763 vs 2757 µg/l, p=0.02); otherwise similar	Yes
Jacobson 2005 US	PEG-IFN at different doses/duration	Fair	Method not described	Yes	Yes	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Kamal (A) 2002 Germany	PEG-IFN + ribavirin vs PEG-IFN monotherapy	Poor	Not randomized	Not randomized	Yes	Yes
Kamal (B) 2005 Egypt	PEG-IFN at different doses/duration	Fair	Method not described	Method not described	Yes	Yes
Khalili 2005 US	PEG-IFN + ribavirin vs PEG-IFN monotherapy	Fair	Method not described	Method not described	NR	Yes
Laguno 2004 Spain	PEG-IFN vs interferon	Fair	Yes	Method not described	Yes	Yes
Lee 2005 Taiwan	PEG-IFN vs interferon	Fair	Yes	Method not described	Yes	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Lodato 2005 Italy	PEG-IFN at different doses/duration	Fair	Method not described	Method not described	Yes	Yes
Mangia (A) 2005 Italy	PEG-IFN vs interferon	Fair	Yes	Yes	No	Yes
Mangia (B) 2005 Italy	PEG-IFN at different doses/duration	Fair	Method not described	Yes	Yes	Yes
Manns 2001 Multiple (Europe, Canada, Argentina, US)	PEG-IFN vs interferon	Fair	Method not described	Yes	Yes	Yes
Mathew 2006 US	PEG-IFN at different doses/duration	Poor	Method not described	Method not described	NR	Yes
Meyer-Wyss 2006 Switzerland	PEG-IFN at different doses/duration	Poor	Method not described	Yes	NR Only reported for 219/232 analyzed	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Poizot-Martin 2003 France	PEG-IFN vs interferon	Poor	Not randomized	Not randomized	No	No
Sanchez-Tapias 2006 Spain	PEG-IFN at different doses/duration	Fair	Yes	Yes	Yes	Yes
Scotto 2005	PEG-IFN vs interferon	Fair	Yes	Method not described	Yes	Yes
Silva 2006 Argentina, Mexico, Germany COMPARE	H2H (early response)	Fair	Method not described	Yes	No	Yes
Sporea 2006 Romania	H2H (early response)	Poor	No	No	Yes	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	Quality Rating	Randomization Adequate	Allocation Concealment Adequate	Groups Similar at Baseline	Eligibility Criteria Specified
Torriani 2004 Multiple APRICOT	PEG-IFN vs interferon	Good	Yes	Yes	Yes	Yes
Tsubota 2005 Japan	PEG-IFN vs interferon	Fair	Method not described	Yes	Yes	Yes
Von Wagner 2005 Germany	PEG-IFN at different doses/duration	Fair	Method not described	Method not described	Yes	Yes
Yu 2006 Taiwan	PEG-IFN at different doses/duration	Fair	Yes	Method not described	Yes	Yes
Zeuzem (A) 2004 Multiple (Australia, Eur, NZ, North and South Am) PEGASYS Study NR16071	PEG-IFN at different doses/duration	Fair	Yes		Yes	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Loss to Followup Differential High	Intention to Treat Analysis
Abergel 2006 France	NR	NR	NR	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	unable to determine	No 1 excluded for protocol violation
Alfaleh 2004 Saudi Arabia	NR	NR	NR	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Arizcorreta 2004 Spain	NR	NR	NR	Attrition: No Crossover: No Adherence: No Contamination: No	No	Yes
Berg 2006 Germany	NR	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Brandao 2006 Brazil	NR	No	No	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	No	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Loss to Followup Differential High	Intention to Treat Analysis
Bruno 2004 Italy	NR	NR	NR	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	No	Yes
Buti 2002 Israel and Spain	NR	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Cargnel 2005 Italy Italian Co-infection Study (ICOS)	NR	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	Yes More dropped out due to 'arbitrary changes in treatment schedule' in arm A (7 vs. 0)	Yes
Carrat 2004 France	Yes	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	Yes	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Loss to Followup Differential High	Intention to Treat Analysis
Chung 2004 US Adult AIDS Clinical Trials Group A5071	NR	NR	NR	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Crespo 2007 Spain	No	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	No 24/121 withdrawal; 1/121 lost to follow-up	Yes
Derbala 2005 Egypt	NR	NR	NR	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	No
El-Zayadi 2005 Egypt	NR	NR	NR	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Fried 2002 Multiple (US, Europe, Australia, Brazil) Pegasys International Study Group	Yes	Yes	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	No	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Loss to Followup Differential High	Intention to Treat Analysis
Glue 2000 France	NR	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	No 66/72 analyzed
Hadziyannis 2004	Yes	Yes	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	No	Yes
Helbling 2006 Switzerland	NR	No	No	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	Yes 3/64 vs. 7/60	Yes
Inati 2005 Lebanon	NR	NR	NR	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Jacobson 2005 US	NR	No	No	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	No	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Loss to Followup Differential High	Intention to Treat Analysis
Kamal (A) 2002 Germany	NR	No	No	Attrition: No Crossover: No Adherence: No Contamination: No	No	Yes
Kamal (B) 2005 Egypt	Unclear, reported as double blind	Unclear, reported as double blind	Unclear, reported as double blind	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Khalili 2005 US	NR	Yes	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Laguno 2004 Spain	No	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Lee 2005 Taiwan	No	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Loss to Followup Differential High	Intention to Treat Analysis
Lodato 2005 Italy	NR	No	No	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	No	Yes
Mangia (A) 2005 Italy	No	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Mangia (B) 2005 Italy	NR	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Manns 2001 Multiple (Europe, Canada, Argentina, US)	No	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Mathew 2006 US	NR	No	No	Attrition: No Crossover: No Adherence: No Contamination: No	Unable to determine	Yes Except for post-randomziation exclusions
Meyer-Wyss 2006 Switzerland	NR	No	No	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	No	No 8/227 excluded for per-protocol analysis

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Loss to Followup Differential High	Intention to Treat Analysis
Poizot-Martin 2003 France	NR	No	No	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Unable to determine
Sanchez-Tapias 2006 Spain	NR	No	No	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	Yes 39 refused or failed to return in 72-week group versus 15 in 48 week group	Yes
Scotto 2005	NR	No	No	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	No	Yes
Silva 2006 Argentina, Mexico, Germany COMPARE	Yes	Yes	Yes	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Sporea 2006 Romania	NR	NR	NR	Attrition: No Crossover: No Adherence: No Contamination: No	Unable to determine	Unable to determine

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Outcome Assessors Masked	Care Provider Masked	Patients Masked	Reporting of Attrition Crossover Adherence and Contamination	Loss to Followup Differential High	Intention to Treat Analysis
Torriani 2004 Multiple APRICOT	Yes	Yes	Yes	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	No	Yes
Tsubota 2005 Japan	NR	NR	NR	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Von Wagner 2005 Germany	NR	NR	NR	Attrition: Yes Crossover: No Adherence: No Contamination: No	No	Yes
Yu 2006 Taiwan	NR	No	No	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	No	Yes
Zeuzem (A) 2004 Multiple (Australia, Eur, NZ, North and South Am) PEGASYS Study NR16071	NR	No	No	Attrition: Yes Crossover: No Adherence: Yes Contamination: No	Yes 14/210 (48 weeks) vs. 1/211 (24 weeks) withdrew due to 'refused treatment'	Yes Except for post-rand exclusions

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Abergel 2006 France	Yes 6/210	Screened: NR Eligible: NR Enrolled: 210	Yes	Schering-Plough
Alfaleh 2004 Saudi Arabia	Yes	Screened: 102 Eligible: NR Enrolled: 96	Yes	Schering-Plough
Arizcorreta 2004 Spain	Unable to determine	Screened: NR Eligible: NR Enrolled: 21	Yes	Not Reported
Berg 2006 Germany	Yes	Screened: 467 Eligible: 459 Enrolled: 459	Yes	Hoffman-LaRoche, Government, and Other
Brandao 2006 Brazil	No	Screened: NR Eligible: NR Enrolled: 117	No	Roche

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Bruno 2004 Italy	Yes	Screened: 430 Eligible: NR Enrolled: 323	Yes	Not Reported. Authors did not receive funding from the pharmaceutical company involved in the manufacture of the study
Buti 2002 Israel and Spain	Unable to determine	Screened: NR Eligible: NR Enrolled: 55	Yes	Schering-Plough
Cargnel 2005 Italy Italian Co-infection Study (ICOS)	No	Screened: NR Eligible: NR Enrolled: 135	Yes	Not reported
Carrat 2004 France	Yes 4 patients who violated entry criteria	Screened: 442 Eligible: 416 Enrolled: 416	Yes	Agence Nationale de Recherches sur le SIDA (publicly funded agency). Drugs provided by Schering Plough

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Chung 2004 US Adult AIDS Clinical Trials Group A5071	Yes 1 patient who did not meet entry criteria	Screened: NR Eligible: NR Enrolled: 134	Yes	National Institue of Allergy and Infectious Diseases and Adult AIDS Clinical Trials Group (ACTG)
Crespo 2007 Spain	No	Screened: 138 Eligible: 125 Enrolled: 121	Yes	Foundation and government (non-industry)
Derbala 2005 Egypt	Yes 9/70 excluded from analyses	Screened: NR Eligible: NR Enrolled: 70	Yes	Not Reported
El-Zayadi 2005 Egypt	Unable to determine	Screened: NR Eligible: NR Enrolled: 180	Yes	Not Reported
Fried 2002 Multiple (US, Europe, Australia, Brazil) Pegasys International Study Group	Yes	Screened: 1459 Eligible: NR Enrolled: 1149		Hoffman-LaRoche

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Glue 2000 France	Unable to determine	Screened: NR Eligible: NR Enrolled: 72	Yes	Schering-Plough
Hadziyannis 2004	Yes 27/1311 did not receive any study med	Screened: 1736 Eligible: NR Enrolled: 1311	Yes	Roche
Helbling 2006 Switzerland	Yes 2/126	Screened: NR Eligible: NR Enrolled: 126	Yes	Roche
Inati 2005 Lebanon	No	Screened: 32 Eligible: 27 Enrolled: 20	Yes	Hoffman-LaRoche
Jacobson 2005 US	No	Screened: 330 Eligible: 321 Enrolled: 321	Yes	Schering-Plough

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Kamal (A) 2002 Germany	Unable to determine	Screened: NR Eligible: NR Enrolled: 42	Yes	Not Reported
Kamal (B) 2005 Egypt	Yes 8/287	Screened: 335 Eligible: 287 Enrolled: 287	Yes	Fullbright Foundation, NIAID, USA, ISID, and Alexander von Humboldt Foundation, Bonn, Germany
Khalili 2005 US	No	Screened: NR Eligible: NR Enrolled: 155	Yes	Roche
Laguno 2004 Spain	Yes 4/99 didn't receive therapy	Screened: 149 Eligible: 120 Enrolled: 95	Yes	Schering Plough, Generalitat de Catalunya, and Red Tematica de Investigacion en SIDA of FISss
Lee 2005 Taiwan	Unable to determine	Screened: NR Eligible: NR Enrolled: NR	Yes	Schering-Plough

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Lodato 2005 Italy	No	Screened: 71 Eligible: 66 Enrolled: 65	Yes	Not reported
Mangia (A) 2005 Italy	No	Screened: NR Eligible: NR Enrolled: 362	Yes	Not Reported
Mangia (B) 2005 Italy	No	Screened: NR Eligible: NR Enrolled: 283	Yes	Investigator-sponsored; no financial support from industry.
Manns 2001 Multiple (Europe, Canada, Argentina, US)	No	Screened: 2316 Eligible: 2057 Enrolled: 1530	Yes	Schering Plough, Massachuttes general Hospital, Scripps Clinic, and University of Florida
Mathew 2006 US	Yes 13/165 withdrew	Screened: NR Eligible: NR Enrolled: 165	Yes	Schering Plough
Meyer-Wyss 2006 Switzerland	Yes 17/231	Screened: NR Eligible: NR Enrolled: 239	Yes	Essex Chemie

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Poizot-Martin 2003 France	Unable to determine	Screened: 341 Eligible: 297 Enrolled: 62		Not Reported
Sanchez-Tapias 2006 Spain	No	Screened: NR Eligible: NR Enrolled: 522	Yes	Roche
Scotto 2005	No	Screened: NR Eligible: NR Enrolled: 78	Yes	Not reported
Silva 2006 Argentina, Mexico, Germany COMPARE	Unable to determine	Screened: NR Eligible: 36 Enrolled: 36	Yes	Schering-Plough
Sporea 2006 Romania	Unable to determine	Screened: NR Eligible: NR Enrolled: 58	No	Not reported. States that study was not supported by any pharmaceutical company producing the PEG-IFNs

Evidence Table 3. Quality assessment of randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Post randomization or Post enrollment Exclusions	Number Screened Eligible Enrolled	Exclusion Criteria Specified	Funding
Torriani 2004 Multiple APRICOT	Yes	Screened: 1158 Eligible: 979 Enrolled: 868	Yes	
Tsubota 2005 Japan	Yes	Screened: NR Eligible: NR Enrolled: 48	Yes	Not reported
Von Wagner 2005 Germany	No	Screened: NR Eligible: NR Enrolled: 153	Yes	Hoffman-LaRoche and German Hepatitis Network of Competence
Yu 2006 Taiwan	No	Screened: 140 Eligible: NR Enrolled: 60	Yes	Taiwan Liver Research Foundation
Zeuzem (A) 2004 Multiple (Australia, Eur, NZ, North and South Am) PEGASYS Study NR16071	Yes 19/459	Screened: NR Eligible: NR Enrolled: 440	Yes	Roche

Evidence Table 4. Adverse events reported in randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	N	Intervention	Ribavirin daily dose	Adverse Events
Silva 2006 Argentina, Mexico, Germany COMPARE	H2H (early response)		36	Peginterferon alfa-2b 1.5 µg/kg 1x / week for 8 weeks	13 mg/kg daily	Withdrawals due to AE: 4/18 (22.22%) Anemia: 10/18 (55.56%) Flu-like symptoms: 5/18 (27.78%) Neutropenia: 10/18 (55.56%) Thrombocytopenia: 3/18 (16.67%)
				Peginterferon alfa-2a 180 µg 1x / week for 8 weeks	13 mg/kg daily	Withdrawals due to AE: 2/18 (11.11%) Anemia: 9/18 (50%) Flu-like symptoms: 3/18 (16.67%) Neutropenia: 12/18 (66.67%) Thrombocytopenia: 5/18 (27.78%)
Sporea 2006 Romania	H2H (early response)		116	Peginterferon alfa-2a 180 µg/kg 1x / week for 12 weeks	800-1200 mg daily	
				Peginterferon alfa-2b 1.5 µg/kg 1x / week for 12 weeks	800-1200 mg daily	
Alfaleh 2004 Saudi Arabia	PEG-IFN vs interferon		96	peginterferon alfa-2b 100 µg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 3/48 (6.25%) Anemia: 35/48 (72.92%) Deaths: 0/48 (0%) Depression: 4/48 (8.33%) Dose reduction: 6/48 (12.5%) Flu-like symptoms: 19/48 (39.58%) Thrombocytopenia: 4/48 (8.33%) Thyroid disease: 8/48 (16.67%) Skin rash: 10/48 (20.83%)

Evidence Table 4. Adverse events reported in randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	N	Intervention	Ribavirin daily dose	Adverse Events
				interferon alfa-2b 3 million units 3x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 1/48 (2.08%) Anemia: 27/48 (56.25%) Deaths: 1/48 (2.08%) Depression: 3/48 (6.25%) Dose reduction: 4/48 (8.33%) Flu-like symptoms: 16/48 (33.33%) Thrombocytopenia: 3/48 (6.25%) Thyroid disease: 3/48 (6.25%) Skin rash: 5/48 (10.42%)
Bruno 2004 Italy	PEG-IFN vs interferon		311	peginterferon alfa-2b 1x/week for 48 weeks	1000-1200 mg daily	Withdrawals due to AE: 20/163 (12.27%) Dose reduction: 76/163 (46.63%) Severe (grade 3 or 4) adverse events: 18/163 (11.04%)
				interferon alfa-2b 6 million units every other day for 48 weeks	1000-1200 mg daily	Withdrawals due to AE: 38/148 (25.68%) Dose reduction: 57/148 (38.51%) Severe (grade 3 or 4) adverse events: 33/148 (22.3%)
Derbala 2005 Egypt	PEG-IFN vs interferon		61	Peginterferon alfa-2b 1.5 µg/kg 1x / week for 48 weeks	800-1200 mg daily	Withdrawals due to AE: 5/30 (16.67%) Dose reduction: 9/30 (30%) Flu-like symptoms: 30/30 (100%)
				Interferon alfa-2b 3 million units 3x / week for 48 weeks	800-1200 mg daily	Withdrawals due to AE: 4/31 (12.9%) Dose reduction: 7/31 (22.58%) Flu-like symptoms: 31/31 (100%)

Evidence Table 4. Adverse events reported in randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	N	Intervention	Ribavirin daily dose	Adverse Events
Lee 2005 Taiwan	PEG-IFN vs interferon		153	Peginterferon alpha-2b 1.5 µg/kg 1x / week for 24 weeks	1000-1200 mg daily	Anemia: 26/76 (34.21%) Deaths: 1/76 (1.32%) Dose reduction: 21/76 (27.63%) Neutropenia: 17/76 (22.37%) Thrombocytopenia: 20/76 (26.32%) anxiety/depression: 21/76 (27.63%)
				Interferon alpha-2b 3 million unit 3x / week for 24 weeks	1000-1200 mg daily	Anemia: 18/77 (23.38%) Deaths: 0/77 (0%) Dose reduction: 9/77 (11.69%) Neutropenia: 5/77 (6.49%) Thrombocytopenia: 8/77 (10.39%) anxiety/depression: 10/77 (12.99%)
Mangia (A) 2005 Italy	PEG-IFN vs interferon		362	Peginterferon alfa-2a (with amantadine) 180 µg 1x / week for 48 weeks	1000-1200 mg daily	Flu-like symptoms: 54/121 (44.63%) Weight loss: 12/121 (9.92%) Psychiatric symptoms: 15/121 (12.4%)
				Interferon alpha-2a (with amantadine) 3 million unit 3x / week for 48 weeks	1000-1200 mg daiily	Flu-like symptoms: 60/120 (50%) Weight loss: 6/120 (5%) Psychiatric symptoms: 16/120 (13.33%)
				Interferon alpha-2a 3 million unit 3x / week for 48 weeks	1000-1200 mg daily	Flu-like symptoms: 53/121 (43.8%) Weight loss: 4/121 (3.31%) Psychiatric symptoms: 20/121 (16.53%)
Manns 2001 Multiple (Europe, Canada, Argentina, US)	PEG-IFN vs interferon		1530	peginterferon alfa-2b (0.5 µg/kg) 0.5 µg/kg 1x / week for 48 weeks	1000-1200 mg daily	Withdrawals due to AE: 67/514 (13.04%) Depression: 149/514 (28.99%) Dose reduction: 185/514 (35.99%)
				peginterferon alfa-2b (1.5 µg/kg) 1.5 ug/kg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 72/511 (14.09%) Depression: 158/511 (30.92%) Dose reduction: 215/511 (42.07%)

Evidence Table 4. Adverse events reported in randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	N	Intervention	Ribavirin daily dose	Adverse Events
				interferon 2b 3 mu 3x / week for 48 weeks	1000-1200 mg daily	Withdrawals due to AE: 66/505 (13.07%) Depression: 172/505 (34.06%) Dose reduction: 172/505 (34.06%)
Scotto 2005	PEG-IFN vs interferon		78	Peginterferon alfa-2b 1.5 µg/kg 1x / week for 52 weeks	800-1200 mg daily	Flu-like symptoms: 15/26 (57.69%) emotional disturbances, mainly depression: 8/26 (30.77%)
				Interferon alfa-2b (3x/week) 6 million units 3x / week for 52 weeks	800-1200 mg daily	Flu-like symptoms: 18/26 (%) emotional disturbances, mainly depression: 9/26 (%)
				Interferon alfa-2b (daily) 3 million units daily for 52 weeks	800-1200 mg daily	Flu-like symptoms: 11/26 (42.31%) emotional disturbances, mainly depression: 5/26 (19.23%)
Tsubota 2005 Japan	PEG-IFN vs interferon		48	Peginterferon alfa-2b 1.5 µg/kg 1x / week for 48 weeks	600-1000 mg daily	
				Interferon alfa-2b 6 million units 3x / week for 48 weeks	600-1000 mg daily	
Arizcorreta 2004 Spain	PEG-IFN vs interferon	HIV subgroup	21	peginterferon alfa-2a 180 µg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 2/11 (18.18%)
				Interferon alfa-2a 3 million units 3x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 2/10 (20%)

Evidence Table 4. Adverse events reported in randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	N	Intervention	Ribavirin daily dose	Adverse Events
Carrat 2004 France	PEG-IFN vs interferon	HIV subgroup	412	peginterferon alfa-2b 1.5 µg/kg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 33/205 (16.1%) Anemia: 1/194 (0.52%) Deaths: 5/194 (2.58%) Depression: 46/194 (23.71%) Dose reduction: 64/194 (32.99%) Flu-like symptoms: 172/194 (88.66%) Neutropenia: 14/194 (7.22%) Thrombocytopenia: 9/194 (4.64%)
				interferon alfa-2b 3 million units 3x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 30/207 (14.49%) Anemia: 1/189 (0.53%) Deaths: 2/189 (1.06%) Depression: 55/189 (29.1%) Dose reduction: 39/189 (20.63%) Flu-like symptoms: 151/189 (79.89%) Neutropenia: 3/189 (1.59%) Thrombocytopenia: 1/189 (0.53%)
Chung 2004 US Adult AIDS Clinical Trials Group A5071	PEG-IFN vs interferon	HIV subgroup	133	peginterferon alfa-2a 180 µg 1x / week for 48 weeks	600-1000 mg daily	Withdrawals due to AE: 8/66 (12.12%) Anemia: 3/66 (4.55%) Depression: 9/66 (13.64%) Flu-like symptoms: 39/66 (59.09%) Neutropenia: 53/66 (80.3%) Thrombocytopenia: 16/66 (24.24%)
				Interferon alfa-2a 3-6 million iu 3x / week for 48 weeks	600-1000 mg daily	Withdrawals due to AE: 8/67 (11.94%) Anemia: 1/67 (1.49%) Depression: 8/67 (11.94%) Flu-like symptoms: 38/67 (56.72%) Neutropenia: 23/67 (34.33%) Thrombocytopenia: 2/67 (2.99%)

Evidence Table 4. Adverse events reported in randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	N	Intervention	Ribavirin daily dose	Adverse Events
Crespo 2007 Spain	PEG-IFN vs interferon	HIV subgroup	121	Peginterferon alfa-2b 1.5 µg/kg 1x / week for 24-48 weeks	800 mg daily	Withdrawals due to AE: 6/60 (10%) Deaths: 0/60 (0%) Dose reduction: 16/60 (%) Flu-like symptoms: 53/60 (88.33%)
				Interferon alfa-2b 3 million units 3x / week for 24-48 weeks	800 mg daily	Withdrawals due to AE: 7/61 (11.48%) Deaths: 2/61 (3.28%) Dose reduction: 0/61 (0%) Flu-like symptoms: 49/61 (80.33%)
Laguno 2004 Spain	PEG-IFN vs interferon	HIV subgroup	95	Peginterferon alpha-2b 100-150 µg 1x / week for 48 weeks	800-1200 mg daily	Withdrawals due to AE: 9/52 (17.31%) Anemia: 16/52 (30.77%) Depression: 19/52 (36.54%) Dose reduction: 22/52 (42.31%) Flu-like symptoms: 46/52 (88.46%) Neutropenia: 14/52 (26.92%) Thrombocytopenia: 13/52 (25%)
				Interferon alpha-2b 3 million units 3x / week for 48 weeks	800-1200 mg daily	Withdrawals due to AE: 5/43 (11.63%) Anemia: 10/43 (23.26%) Depression: 22/43 (51.16%) Dose reduction: 16/43 (37.21%) Flu-like symptoms: 32/43 (74.42%) Neutropenia: 7/43 (16.28%) Thrombocytopenia: 6/43 (13.95%)
Poizot-Martin 2003 France	PEG-IFN vs interferon	HIV subgroup	62	Peginterferon alfa-2b 180 µg 1x / week for 6-12 months	1600 mg daily	
				Interferon alfa-2b 3 million units 3x / week for 6-12 months	1600 mg daily	

Evidence Table 4. Adverse events reported in randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	N	Intervention	Ribavirin daily dose	Adverse Events
Torriani 2004 Multiple APRICOT	PEG-IFN vs interferon	HIV subgroup	860	Peginterferon alfa-2a 180 µg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 34/290 (11.72%) Anemia: 6/288 (2.08%) Depression: 76/288 (26.39%) Thrombocytopenia: 1/288 (0.35%) Dose reduction due to adverse event: 30/288 (10.42%) Dose reduction due to laboratory abnormality: 97/288 (33.68%)
				Peginterferon alfa-2a (no ribavirin) 180 ug 1x / week for 48 weeks		Withdrawals due to AE: 34/289 (11.76%) Anemia: 6/286 (2.1%) Depression: 57/286 (19.93%) Thrombocytopenia: 4/286 (1.4%) Dose reduction due to adverse event: 21/286 (7.34%) Dose reduction due to laboratory abnormality (anemia, neutropenia, thrombocytopenia, other): 94/286 (32.87%)
				Interferon alfa-2a 3 million units 3x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 41/289 (14.19%) Anemia: 3/285 (1.05%) Depression: 64/285 (22.46%) Thrombocytopenia: 0/286 (0%) Dose reduction due to adverse event: 33/285 (11.58%) Dose reduction due to laboratory abnormality (anemia, neutropenia, thrombocytopenia, other): 18/285 (6.32%)

Evidence Table 4. Adverse events reported in randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	N	Intervention	Ribavirin daily dose	Adverse Events
Fried 2002 Multiple (US, Europe, Australia, Brazil) Pegasys International Study Group	PEG-IFN + ribavirin vs PEG-IFN monotherapy		1121	Peginterferon alfa-2a 180 µg 1x / week for 48 weeks	1000-1200 mg daily	Withdrawals due to AE: 32/453 (7.06%) Depression: 100/451 (22.17%) Dose reduction for adverse event: 48/451 (10.64%) Dose reduction for laboratory abnormality (anemia, neutropenia, thrombocytopenia): 111/451 (24.61%)
				Interferon alfa-2b 3 million unit 3x / week for 48 weeks	1000-1200 mg daily	Withdrawals due to AE: 43/444 (9.68%) Deaths: 1/444 (0.23%) Depression: 134/443 (30.25%) Dose reduction for adverse event: 47/443 (10.61%) Dose reduction for laboratory abnormality (anemia, neutropenia, thrombocytopenia): 36/443 (8.13%)
				Peginterferon alfa-2a (no ribavirin) 180 µg 1x / week for 48 weeks		Withdrawals due to AE: 13/224 (5.8%) Depression: 45/223 (20.18%) Dose reduction for adverse event: 14/223 (6.28%) Dose reduction for laboratory abnormality (anemia, neutropenia, thrombocytopenia): 54/223 (24.22%)
Inati 2005 Lebanon	PEG-IFN + ribavirin vs PEG-IFN monotherapy		20	Peginterferon alfa-2a (plus placebo) 180 µg 1x / week for 48 weeks		
				Peginterferon alfa-2a (plus ribavirin) 180 µg 1x / week for 48 weeks	10.6 mg/kg daily	

Evidence Table 4. Adverse events reported in randomized controlled trials of pegylated interferons for chronic hepatitis C infection

Study	Trial Type	HIV	N	Intervention	Ribavirin daily dose	Adverse Events
Kamal (A) 2002 Germany	PEG-IFN + ribavirin vs PEG-IFN monotherapy		42	Peginterferon alfa-2a 180 µg 1x / week for 48 weeks	800-1200 mg daily	
				Peginterferon alfa-2a 180 µg 1x / week for 48 weeks		
				Interferon alfa-2a 3-6 million units 3x / week for 48 weeks		
Cargnel 2005 Italy Italian Co-infection Study (ICOS)	PEG-IFN + ribavirin vs PEG-IFN monotherapy	HIV subgroup	135	Peginterferon alfa-2b (plus ribavirin) 1.5 µg/kg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 15/69 (21.74%) Dose reduction: 12/69 (17.39%) Flu-like symptoms: 15/69 (21.74%) Psychiatric disorders: 4/69 (5.8%) Hematological toxicity: 13/69 (18.84%)
				Peginterferon alfa-2b monotherapy 1.5 µg/kg 1x / week for 48 weeks		Withdrawals due to AE: 15/66 (22.73%) Dose reduction: 8/66 (12.12%) Flu-like symptoms: 2/66 (3.03%) Psychiatric disorders: 3/66 (4.55%) Hematological toxicity: 10/66 (15.15%)
Khalili 2005 US	PEG-IFN + ribavirin vs PEG-IFN monotherapy	HIV subgroup	154	Peginterferon alfa-2a (plus ribavirin) 180 mg 1x / week for 48 weeks	800 mg daily	Depression: 6/37 (16.22%) Neutropenia: 2/37 (5.41%)
				Peginterferon alfa-2a (plus placebo) 180 mg 1x / week for 48 weeks		Depression: 7/39 (17.95%) Neutropenia: 1/39 (2.56%)

Evidence Table 5. Adverse events reported in dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	N	Treatment History	Intervention	Ribavirin daily dose	Adverse Events
Abergel 2006 France	203	Treatment naïve	Peginterferon alfa-2b (1.5 µg/kg) 1.5 µg/kg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 8/101 (7.92%) Anemia: 9/101 (8.91%) Depression: 13/101 (12.87%) Dose reduction: 36/101 (35.64%) Neutropenia: 10/101 (9.9%) Thrombocytopenia: 3/101 (2.97%) Suicide: 2/101 (1.98%) Hypothyroidism: 9/101 (8.91%)
			Peginterferon alfa-2b (0.75 µg/kg) 0.75 µg/kg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 4/102 (3.92%) Anemia: 5/102 (4.9%) Depression: 15/102 (14.71%) Dose reduction: 13/102 (12.75%) Neutropenia: 4/102 (3.92%) Thrombocytopenia: 0/102 (0%) Suicide: 0/102 (0%) Hypothyroidism: 1/102 (0.98%)
Berg 2006 Germany	455	Treatment naïve	Peginterferon alfa-2a (48 weeks) 180 µg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 21/230 (9.13%) Dose reduction: 76/230 (33.04%) Serious AEs: 36/230 (15.65%)
			Peginterferon alfa-2a (72 weeks) 180 µg 1x / week for 72 weeks	800 mg daily	Withdrawals due to AE: 26/225 (11.56%) Dose reduction: 82/225 (36.44%) Serious AEs: 25/225 (11.11%)
Brandao 2006 Brazil	117	Treatment naïve	Peginterferon alfa-2a (genotype 1, 24 weeks) 180 µg 1x / week for 24 weeks	800 mg daily	Withdrawals due to AE: 2/32 (6.25%) Deaths: 0/32 (0%) Depression: 5/32 (15.62%) Dose reduction: 3/32 (9.38%) Flu-like symptoms: 8/32 (25%) Neutropenia: 8/32 (25%) Thrombocytopenia: 3/32 (9.38%)

Evidence Table 5. Adverse events reported in dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	N	Treatment History	Intervention	Ribavirin daily dose	Adverse Events
			Peginterferon alfa-2a (genotype 1, 48 weeks) 180 µg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 0/31 (0%) Deaths: 0/31 (0%) Depression: 5/31 (16.13%) Dose reduction: 9/31 (29.03%) Flu-like symptoms: 10/31 (32.26%) Neutropenia: 14/31 (45.16%) Thrombocytopenia: 7/31 (22.58%)
			Peginterferon alfa-2a (genotype non-1, 24 weeks) 180 µg 1x / week for 24 weeks	800 mg daily	Withdrawals due to AE: 2/54 (3.7%) Deaths: 0/54 (0%) Depression: 5/54 (9.26%) Dose reduction: 8/54 (14.81%) Flu-like symptoms: 29/54 (53.7%) Neutropenia: 23/54 (42.59%) Thrombocytopenia: 14/54 (25.93%)
Buti 2002 Israel and Spain	55	Treatment naïve	Peginterferon alfa-2b (high dose) 1.0 µg/kg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 4/28 (14.29%) Dose reduction: 1/28 (3.57%)
			Peginterferon alfa-2b (low dose) 0.5 µg/kg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 2/27 (7.41%) Dose reduction: 1/27 (3.7%)
El-Zayadi 2005 Egypt	180	Treatment naïve	Peginterferon alfa-2b (48 weeks) 100 µg 1x / week for 48 weeks	1000-1200 mg daily	Withdrawals due to AE: 2/40 (5%) Flu-like symptoms: 28/40 (70%) cytopenia (neutropenia and thrombocytopenia): 12/40 (30%) psychological disorders: 5/40 (12.5%)

Evidence Table 5. Adverse events reported in dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	N	Treatment History	Intervention	Ribavirin daily dose	Adverse Events
			Peginterferon alpha-2b (24 weeks) 100 ug 1x / week for 24 weeks	1000-1200 mg daily	Withdrawals due to AE: 2/70 (2.86%) Flu-like symptoms: 51/70 (72.86%) cytopenia (neutropenia and thrombocytopenia): 21/70 (30%) psychological disorders: 6/70 (8.57%)
			Interferon alpha-2b 3 million unit daily for 24 weeks	1000-1200 mg daily-1x/week	Withdrawals due to AE: 2/70 (2.86%) Flu-like symptoms: 50/70 (71.43%) cytopenia (neutropenia and thrombocytopenia): 18/70 (25.71%) psychological disorders: 4/70 (5.71%)
Glue 2000 France	72	Treatment naïve	Peginterferon alfa-2b (0.35 + RBV) 0.35 µg/kg 1x / week for 24 weeks	800-1200 mg daily	
			Peginterferon alfa-2b (0.35 alone) 0.35 µg/kg 1x / week for 24 weeks		
			Peginterferon alfa-2b (0.7 + RBV) 0.7 µg/kg 1x / week for 24 weeks	800-1200 mg daily	
			Peginterferon alfa-2b (0.7 alone) 0.7 µg/kg 1x / week for 24 weeks		
			Peginterferon alfa-2b (1.4 + RBV) 1.4 µg/kg 1x / week for 24 weeks	800-1200 mg daily	

Evidence Table 5. Adverse events reported in dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	N	Treatment History	Intervention	Ribavirin daily dose	Adverse Events
			Peginterferon alfa-2b (1.4 alone) 1.4 µg/kg 1x / week for 24 weeks		
			Peginterferon alfa-2b (0.7 alone)		
			Peginterferon alfa-2b (1.4 + RBV)		
			Peginterferon alfa-2b (1.4 alone)		
Hadziyannis 2004	1284	Treatment naïve	Peginterferon alfa-2a (24 weeks, low dose RBV) 180 µg 1x / week for 24 weeks	800 mg daily	Withdrawals due to AE: 10/207 (4.83%) Deaths: 0/207 (0%) Depression: 43/207 (20.77%) Dose reduction: 63/207 (30.43%)
			Peginterferon alfa-2a (24 weeks, standard RBV) 180 µg 1x / week for 24 weeks	1000-1200 mg daily	Withdrawals due to AE: 13/280 (4.64%) Deaths: 1/280 (0.36%) Depression: 42/280 (15%) Dose reduction: 73/280 (26.07%)
			Peginterferon alfa-2a (48 weeks, low dose RBV) 180 µg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 59/361 (16.34%) Deaths: 1/361 (0.28%) Depression: 79/361 (21.88%) Dose reduction: 120/361 (33.24%)

Evidence Table 5. Adverse events reported in dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	N	Treatment History	Intervention	Ribavirin daily dose	Adverse Events
			Peginterferon alfa-2a (48 weeks, standard RBV) 180 µg 1x / week for 48 weeks	1000-1200 mg daily	Withdrawals due to AE: 67/444 (15.09%) Deaths: 2/436 (0.46%) Depression: 104/436 (23.85%) Dose reduction: 159/436 (36.47%)
Helbling 2006 Switzerland	124	Not reported	Peginterferon alfa-2a (standard RBV) 180 µg 1x / week for 48 weeks	1000-1200 mg daily	Withdrawals due to AE: 15/64 (23.44%) Deaths: 0/64 (0%) Dose reduction: 50/64 (78.12%) Psychiatric AEs: 1/64 (1.56%)
			Peginterferon alfa-2a (low RBV) 180 µg 1x / week for 48 weeks	600-800 mg daily	Withdrawals due to AE: 16/60 (26.67%) Deaths: 2/60 (3.33%) Dose reduction: 34/60 (56.67%) Psychiatric AEs: 4/60 (6.67%)
Jacobson 2005 US	321	See comment	Peginterferon alfa-2b (higher dose) 1.5 µg/kg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 21/160 (13.12%) Seroius AEs: 13/160 (8.12%)
			Peginterferon alfa-2b (lower dose) 1.0 µg/kg 1x / week for 48 weeks	1000-1200 mg daily	Withdrawals due to AE: 18/161 (11.18%) Serious AEs: 18/161 (11.18%)
Kamal (B) 2005 Egypt			Peginterferon alfa-2b (24 weeks) 1.5 µg/kg 1x / week for 24 weeks	10.6 mg/kg daily	Withdrawals due to AE: 1/95 (1.05%) Depression: 3/95 (3.16%) Dose reduction: 5/95 (5.26%) Flu-like symptoms: 53/95 (55.79%)
			Peginterferon alfa-2b (24 weeks) 1.5 µg/kg 1x / week for 24 weeks	10.6 mg/kg daily	Withdrawals due to AE: 1/95 (1.05%) Depression: 3/95 (3.16%) Dose reduction: 5/95 (5.26%) Flu-like symptoms: 53/95 (55.79%)

Evidence Table 5. Adverse events reported in dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	N	Treatment History	Intervention	Ribavirin daily dose	Adverse Events
			Peginterferon alfa-2b (36 weeks) 1.5 µg/kg 1x / week for 36 weeks	10.6 mg/kg daily	Withdrawals due to AE: 2/96 (2.08%) Depression: 3/96 (3.12%) Dose reduction: 11/96 (11.46%) Flu-like symptoms: 58/96 (60.42%)
			Peginterferon alfa-2b (36 weeks) 1.5 µg/kg 1x / week for 36 weeks	10.6 mg/kg daily	Withdrawals due to AE: 2/96 (2.08%) Depression: 3/96 (3.12%) Dose reduction: 11/96 (11.46%) Flu-like symptoms: 58/96 (60.42%)
			Peginterferon alfa-2b (48 weeks) 1.5 µg/kg 1x / week for 48 weeks	10.6 mg/kg daily	Withdrawals due to AE: 4/96 (4.17%) Depression: 9/96 (9.38%) Dose reduction: 12/96 (12.5%) Flu-like symptoms: 59/96 (61.46%)
			Peginterferon alfa-2b (48 weeks) 1.5 µg/kg 1x / week for 48 weeks	10.6 mg/kg daily	Withdrawals due to AE: 4/96 (4.17%) Depression: 9/96 (9.38%) Dose reduction: 12/96 (12.5%) Flu-like symptoms: 59/96 (61.46%)
Lodato 2005 Italy	65	40% naïve, 33.8% non-responders, 26.2% relapsers	Peginterferon alfa-2b (1x/week) 1.5 µg/kg 1x / week for 24-48 weeks	10.6 mg/kg daily	Anemia: 2/22 (9.09%) Depression: 4/22 (18.18%) Flu-like symptoms: 15/22 (68.18%)
			Peginterferon alfa-2b (2x/week) 1.5 µg/kg 2x / week for 24-48 weeks	10.6 mg/kg daily	Anemia: 2/43 (4.65%) Depression: 8/43 (18.6%) Flu-like symptoms: 25/43 (58.14%)
Mangia (B) 2005 Italy	283	Treatment naïve	Peginterferon alfa-2b (standard duration) 1.0 µg/kg 1x / week for 24 weeks	1000-1200 mg daily	Withdrawals due to AE: 8/70 (11.43%)

Evidence Table 5. Adverse events reported in dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	N	Treatment History	Intervention	Ribavirin daily dose	Adverse Events
			Peginterferon alfa-2b (variable duration) 1.0 µg/kg 1x / week for 12 or 24 weeks	1000-1200 mg daily	Withdrawals due to AE: 1/213 (0.47%)
Mathew 2006 US	152	63% nonresponder, 30% relapser, 7% unavailable	Peginterferon alfa-2b (high dose) 1.5 µg/kg 1x / week for 48 weeks	1000-1200 mg daily	
			Peginterferon alfa-2b (low dose) 0.5 µg/kg 1x / week for 48 weeks	1000-1200 mg daily	
Meyer-Wyss 2006 Switzerland	219	Treatment naïve	Peginterferon alfa-2b (1.0 µg/kg) 1.0 µg/kg 1x / week for 24-48 weeks	800 mg daily	Withdrawals due to AE: 14/115 (12.17%) Anemia: 3/115 (2.61%) Deaths: 1/115 (0.87%) Dose reduction: 48/115 (42.48%) Thrombocytopenia: 3/115 (2.61%)
			Peginterferon alfa-2b (1.5 µg/kg) 1.5 µg/kg 1x / week for 24-48 weeks	800 mg daily	Withdrawals due to AE: 28/112 (25%) Anemia: 4/112 (3.57%) Deaths: 0/112 (0%) Dose reduction: 63/112 (59.43%) Thrombocytopenia: 5/112 (4.46%)
Sanchez-Tapias 2006 Spain	326	Treatment naïve	Peginterferon alfa-2a (48 weeks) 180 µg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 14/165 (8.48%) Anemia: 30/165 (18.18%) Depression: 19/165 (11.52%) Dose reduction: 41/165 (24.85%) Flu-like symptoms: 39/165 (23.64%) Neutropenia: 40/165 (24.24%) Thrombocytopenia: 22/165 (13.33%)

Evidence Table 5. Adverse events reported in dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	N	Treatment History	Intervention	Ribavirin daily dose	Adverse Events
			Peginterferon alfa-2a (72 weeks) 180 µg 1x / week for 72 weeks	800 mg daily	Withdrawals due to AE: 19/161 (11.8%) Anemia: 34/161 (21.12%) Depression: 31/161 (19.25%) Dose reduction: 49/161 (30.43%) Flu-like symptoms: 28/161 (17.39%) Neutropenia: 41/161 (25.47%) Thrombocytopenia: 14/161 (8.7%)
Von Wagner 2005 Germany	153	Treatment naïve	Peginterferon alfa-2a (16 weeks) 180 µg 1x / week for 16 weeks	800-1200 mg daily	Withdrawals due to AE: 0/71 (0%) Depression: 8/71 (11.27%) Dose reduction: 5/71 (7.04%) Flu-like symptoms: 37/71 (52.11%)
			Peginterferon alfa-2a (24 weeks) 180 µg 1x / week for 24 weeks	800-1200 mg daily	Withdrawals due to AE: 1/71 (1.41%) Depression: 10/71 (14.08%) Dose reduction: 13/71 (18.31%) Flu-like symptoms: 33/71 (46.48%)
Yu 2006 Taiwan	60	Treatment naïve	Peginterferon alfa-2b (24 weeks) 80-100 µg 1x / week for 24 weeks	1000-1200 mg daily	Withdrawals due to AE: 1/45 (2.22%) Anemia: 20/45 (44.44%) Dose reduction: 7/45 (15.56%) Thrombocytopenia: 20/45 (44.44%) Anxiety/depression: 19/45 (42.22%)
			Peginterferon alfa-2b (48 weeks) 80-100 µg 1x / week for 48 weeks	1000-1200 mg daily	Withdrawals due to AE: 2/15 (13.33%) Anemia: 8/15 (53.33%) Dose reduction: 3/15 (20%) Thrombocytopenia: 4/15 (26.67%) Anxiety/depression: 8/15 (53.33%)

Evidence Table 5. Adverse events reported in dose- or duration-ranging trials of pegylated interferons for chronic hepatitis C infection

Study	N	Treatment History	Intervention	Ribavirin daily dose	Adverse Events
Zeuzem (A) 2004 Multiple (Australia, Eur, NZ, North and South Am) PEGASYS Study NR16071	491	Treatment naïve	Peginterferon alfa-2a (24 weeks) 180 µg 1x / week for 24 weeks	800 mg daily	Withdrawals due to AE: 15/212 (7.08%) Deaths: 0/212 (0%) Dose reduction: 23/212 (10.85%)
			Peginterferon alfa-2a (48 weeks) 180 µg 1x / week for 48 weeks	800 mg daily	Withdrawals due to AE: 38/210 (18.1%) Deaths: 0/210 (0%) Dose reduction: 40/210 (19.05%)
			No treatment control for 72 weeks		Deaths: 1/69 (1.45%)
Zeuzem (B) 2005		Treatment naïve	Peginterferon alfa-2a (individualized treatment) See comment		Anemia: 29/136 (21.32%) Depression: 4/136 (2.94%) Dose reduction: 69/136 (50.74%) Neutropenia: 36/136 (26.47%) Thrombocytopenia: 4/136 (2.94%)
			Peginterferon alfa-2a (standard treatment) 180 µg 1x / week for 48 weeks	1000-1200 mg daily	Anemia: 31/134 (23.13%) Depression: 5/134 (3.73%) Dose reduction: 79/134 (58.96%) Neutropenia: 46/134 (34.33%) Thrombocytopenia: 7/134 (5.22%)

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Study of both peginterferon alfa-2a and alfa-2b								
DeLuca, 2004	Before-after	36	alfa-2a or alfa-2b	alfa-2a: 180 µg/week, alfa-2b: 1.5 µg/kg/week	>=11mg/kg	HIV infection	24 weeks	up to 72 weeks
Studies of peginterferon alfa-2a								
Gallegos-Orozco, 2005	Before-after	18	alfa-2a	1.5 µg/kg 1x/week for 4 weeks, then 0.5 µg/week	1000-1200 mg (weight-based)	Chronic HCV	48 weeks	24 weeks post-treatment

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Gheorghe, 2005	Before-after	174	alfa-2a	180 µg 1x/week	1000-1200 mg (weight-based)	75.3% treatment naïve, 14.9% relapsers, 9.8% non-responders	48 weeks	24 weeks post-treatment

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Jeffers, 2004	Before-after	106	alfa-2a	180 µg 1x/week	1000-1200 mg (weight-based)	Blacks (n=78) and whites (n=28)	48 weeks	72 weeks
Juarez-Navarro, 2005	Before-after	209	alfa-2a	180 µg/week	800 mg for genotype non-1, 1000-1200 mg in genotype 1	excluding those with existing neutropenia and cirrhosis	24-48 weeks, depending on genotype	4 weeks after completion of therapy
Lee, 2006	Before-after	508	alfa-2a	180 µg/week	no RBV or 800 mg	34.3% cirrhotic	24 or 48 weeks	72 weeks

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Lindahl, 2005	Before-after	10	alfa-2a	180 µg/week	mean 2540 mg (range 1600-3600 mg); erythropoietin 9000-30,000 IU/week.	Viral load >800,000 IU/mL	48 weeks	24 weeks post-treatment
Shiffman, 2004	Before-after	573	alfa-2a	180 µg 1x/week	1000-1200 mg (weight-based)	Nonresponders to standard interferon, with or without ribavirin	48 weeks	72 weeks

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Sulkowski, 2002	Before-after	20	alfa-2a	180 µg 1x/week	1000-1200 mg (weight-based)	Chronic HCV	24-48 weeks (48 weeks for genotype 1 and VR at week 24)	12 weeks post-treatment
Vere, 2005	Before-after	37	alfa-2a	180 µg 1x/week	1000-1200 mg (weight-based)	Chronic HCV	48 weeks	24 weeks post-treatment
Studies of peginterferon alfa-2b								

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Bagheri, 2004	Prospective, pharmacovigilance	87	alfa-2b	1.5 µg/kg/week	800-1200 mg (weight-based)	19.6% HIV co-infection, 29.4% genotype 1b, 23.5% genotype 1a, 33.3% had received non-pegylated interferon plus ribavirin	48 weeks	One year
Ballesteros, 2004	Before-after	28	alfa-2b	1.5 µg/kg 1x/week	800 mg	HIV infection	24 weeks for HCV genotype 3, 48 weeks for genotypes 1 and 4	12 weeks post-treatment
Cacoub, 2005	Before-after	9	alfa-2b	1.5 µg/kg 1x/week	800-1200 mg (weight-based)	Mixed cryoglobulinemia	Mean 13.5 months (SD 2.8 months, range 10-26 months)	Mean 18.6 months (range 6-33 months)

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Carnicer, 2005	Before-after	124	alfa-2b	1.5 µg/kg 1x/week	Not reported (weight-based)	Non-responders to standard IFN therapy	24 weeks	72 weeks
Chang, 2005	Before-after	115	alfa-2b	Not reported	Not reported (weight-based)	Past alcohol consumption	24-48 weeks depending on HCV genotype	24 weeks post-treatment
Dalgard, 2004	Before-after	122	alfa-2b	1.5 µg/kg 1x/week	800-1400 mg (weight-based)	Genotype 2 or 3	14 weeks (n=95) or 24 weeks (if no early VR, n=27)	24 weeks post-treatment
Dan, 2006 US	Prospective cohort	271	alfa-2b	Not reported	Not reported	31.6% cirrhosis.	48 weeks	24 weeks after treatment completion

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Farel, 2004	Prospective cohort	23	alfa-2b	1.5 µg/kg/week	1000-1200 mg	HIV co-infection	48 weeks	40-88 weeks
Gilleece, 2005	Before-after	27	alfa-2b	1.5 µg/kg 1x/week	800-1200 mg (weight-based)	HIV positive men who have sex with men	24 weeks	48 weeks
Glesby, 2005	Before-after	23	alfa-2b	1.5 µg/kg 1x/week	800-1400 mg (weight based) Also interleukin-2 for 60 weeks	HIV infection	48 weeks	84 weeks
Hasan, 2004	Before-after	66	alfa-2b	1.5 µg/kg 1x/week	1000-1200 mg (weight-based)	Middle Eastern patients infected mainly with HCV genotype 4	48 weeks	24 weeks post-treatment

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Kraus, 2005		98	alfa 2b	1.5 µg/kg/week	800-1200 mg (weight-based)		6-12 months, depending on genotype	4 weeks after completion of therapy
Marrache, 2005	Before-after	80	alfa-2b	0.5 to 1.5 µg/kg/week	800-1200 mg (weight-based)	Bridging fibrosis or cirrhosis	24 weeks for treatment-naïve patients with HCV genotype 2 or 3 (36%), 48 weeks for others	24 weeks post-treatment

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Mauss, 2004	Before-after	100	alfa-2b	1.5 µg/kg 1x/week	1000-1200 mg (weight-based)	On methadone maintenance	24 weeks for HCV genotype 2 and 3, 48 weeks for genotype 1	24 weeks post-treatment
Mazzaro, 2005	Before-after	18	alfa-2b	1.0 µg/kg 1x/week	1000 mg	Mixed cryoglobulinemia	48 weeks	6 months post-treatment

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Moreno Planas, 2005	Before-after	19	alfa-2b	1.5 µg/kg 1x/week	10.6 g/kg	Biopsy-proven cirrhosis (63.2%) or previous cirrhotic complications (26.3%)	24 weeks for HCV genotype 2 and 3 and 48 weeks for genotype 1	Mean 21 months
Moreno, 2004	Before-after	35	alfa-2b	50 µg 1x/week	800 mg	HIV-infected	48 weeks	72 weeks

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Moreno, 2005	Before-after	120	alfa-2b	1.5 µg/kg 1x/week	at least 10.6 mg/kg	HIV-infected, HCV genotype 1; 15.8% liver transplant recipients	24-48 weeks	72 weeks or until treatment discontinuation
Muir, 2004	Before-after	200	alfa-2b	1.5 µg/kg 1x/week	1000 mg first 12 weeks, then 800 mg	Blacks and non-Hispanic whites	48 weeks	72 weeks

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Myers, 2004	Before-after	32	alfa-2b	1.5 µg/kg 1x/week	1000-1200 mg (weight-based)	HIV-infected, nonresponders to and relapsers to standard interferon	48 weeks	72 weeks
Perez-Olmeda, 2003	Before-after	68	alfa-2b	150 µg/week for the first 12 weeks and 100 µg thereafter	800 mg	Chronic HCV	6 months for genotype 2 or 3, 12 months for genotypes 1 or 4.	6-12 months

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Raison, 2005		162	alfa 2b	1.5 µg/kg/week	800 mg (fixed dose) or 1000-1200 mg (weight-based)	Compensated liver disease, treatment naïve 58% men, 88% non-Hispanic white, mean age 45.0 (SD 6.7, range 18-70). 77% genotype 1.	24 weeks	24 weeks
Santin, 2006	Before-after	60	alfa-2b	80-150 µg 1x/week (weight-based)	800-1200 mg (weight-based)	HIV-infected	24-48 weeks	48-72 weeks
Seow, 2005	Before-after	33	alfa-2b	1.5 µg/kg 1x/week	>10.6 mg/kg	Chronic HCV	24 weeks for HCV genotype 2 and 3 and 48 weeks for genotype 1	24 weeks post-treatment

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Seyam, 2005	Retrospective cohort	126	alfa 2b	1.0 to 1.5 µg/kg/week	1000-1200 mg (weight-based)		48 weeks for genotype 1, 4, 5, and 6, 24 weeks for genotypes 2 and 3	24 or 48 weeks (end of treatment)
Taliani, 2006	Before-after	143	alfa-2b	1.5 µg/kg 1x/week	1000-1200 mg (weight-based)	Nonresponders to a previous course of interferon and ribavirin	48 weeks	48 weeks

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Voigt, 2006	Before-after	122	alfa-2b	1.5 µg/kg 1x/week	800 mg	HIV infection	48 weeks for HCV genotypes 1 and 4, and 24 weeks for genotypes 2 and 3	24 weeks post-treatment
Younossi, 2005	Before-after	168	alfa-2b	1.5 µg/kg/week	1000-1200 mg; also amantadine 200 mg	58.9% nonresponders to previous treatment, 41.1% treatment-naïve	24-48 weeks	24 weeks post-treatment

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Study design	N	PEG-IFN	Dose	Ribavirin daily dose; other drugs	Population	Duration of treatment	Duration of followup
Zeuzem, 2004	Before-after	235	alfa-2b	1.5 µg/kg 1x/week	800-1400 mg (weight based)	Low pretreatment viremia (<=600,000 IU/mL)	24 weeks	48 weeks
Zeuzem, 2006	Before-after	235	alfa-2b	1.5 µg/kg 1x/week	800-1400 mg	Low baseline HCV-RNA level (<=600,000 IU/mL	24 weeks	24 weeks

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Study of b alfa-2		
DeLuca, 2004	42% discontinued treatment, occurred at median of 27 weeks (range 3-42 weeks). Type of PEG-IFN was not associated with discontinuation.	None reported
Studies of p		
Gallegos-Orozco, 2005	1 treatment discontinuation due to thyrotoxicosis.	Dose reduction of PEG-IFN in 1 patient due to neutropenia.

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Gheorghe, 2005	Definitive discontinuation in 5.74%. Causes of treatment discontinuation: severe hematological abnormalities, severe and protracted skin rash, resistance to therapy, personal reasons, and 1 case of acute cytomegalic virus hepatitis.	Specific AEs: weight loss 69.9%, fatigue 56.3%, arthralgia 54.6%, pyrexia/chills 52.3%, myalgia 50.6%, irritability 50.4%, decreased appetite 43.5%, prutitis 40.5%, indomnia 38.2%, dry cough 35.1%, depression 33.6%, dry mouth 33.6%, headache 32.87%, alopecia 32.1%, inflammation reaction at injection site 31.6%, skin rash/dermatitis 25.2%, abdominal pain 23.7%, visual disturbances 17.6%, impaired concentration/memory 16.0%, nausea/vomiting 14.9%, epistaxis 13.8%, diarrhea 13.7%, stomatitis 13.0%, taste disturbances 13.0%, infectious complications 8.7%. Mean weight loss index 0.95 +/- 1.11 kg Temporary discontinuation of therapy in 2.15% 9.2% required temporary PEG-IFN dose reduction due to neutropenia and thrombocytopenia. Severe anemia requiring blood transfusion occurred in 1.1%, moderate anemia (8-10 g/dl) in 20.1%. 2 severe life-threatening cases of infectious complications (left deltoid necrotizing faciitis, bilateral orchiepididimitis).

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Jeffers, 2004	Not reported	Incidence rates for AEs higher among whites than blacks, with injection site erythema, vomiting, alopecia, dry skin, and sinusitis having a threefold geater frequency in whites than blacks. One death in a black patient (MI, 180 days after last dose of medication, not considered drug-related). Specific AEs, (blacks vs whites): fatigue 60% vs 71%, headache 54% vs 82%, rigors 35% vs 32%, insomnia 27% vs 50%, rash 26% vs 18%, nausea 23% vs 54%, arthralgia 23% vs 21%, myalgia 22% vs 32%, pyrexia 19% vs 25%, anorexia 19% vs 11%, pain 18% vs 21%, pruritis 18% vs 21%, back pain 18% vs 18%, depression 17% vs 29%, influenza-like illness 17% vs 7%, cough 15% vs 11%, dizziness (including vertigo) 13% vs 29%, dyspnea 12% vs 25%, abdominal pain (upper) 12% vs 21%, diarrhea 12% vs 21%, irritability 10% vs 29%, pharyngeal pain 10% vs 21%, alopecia 6% vs 32%, dry mouth 6% vs 18%, injection-site erythema 5% vs 29%, dry skin 4% vs 25%, vomiting 4% vs 21%, sinusitis 3% vs 18%.
Juarez-Navarro, 2005	Not reported	Measured infections and neutropenia: 54.5% did not develop neutropenia; 45.5% had neutrophil count <1500 cells/µl; 96.8% 750-1500 cells/µl; 3.2% 500-750 cells/µl; and none <500 cells/µl. Infection rates were 17%, 33.3%, and 0% for 750-1499; 500-749, and <500 cells/cells/µl; respectively
Lee, 2006	32% of non-cirrhotic and 40% of cirrhotic patients prematurely discontinued treatment. AEs accounted for discontinuation in <=8% of patients in the combination therapy groups.	Incidence of AEs was similar in cirrhotic and non-cirrhotic patients and across treatment arms. Overall AEs: 44.7%, Serious AEs: 4.7%, non-serious laboratory abnormalities 30.7%, neutropenia (grade 3): 15.4%, neutropenia (grade 4): 2.2%, neutropenia (not graded): 2.6%, thrombocytopenia (grade 3): 2.2%, thrombocytopenia (not graded): 2.2%, anemia (<10 g/dL): 9.1%, anemia (>=10 g/dL): 2.2%, ALT elevation: 2.0%

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Lindahl, 2005	One discontinuation of ribavirin due to side effects. 4 patients discontinued PEG-IFN for a short period or a reduced dose was given due to neutropenia.	Hemoglobin levels decreased. 2 dose reductions of ribavirin due to decrease in hemoglobin. Nausea caused a minor dose reduction in one additional patients. Working capacity was reduced in all patients. 1 relapse of amphetamine use. Mean weight (range) at baseline, treatment week 12 and treatment week 20 was 80.6 (66.5-109.0), 79.0 (63.5-110.0), and 78.0 (62.9-110.0). Specific AEs: fatigue 100%, pruritus or dermatitis 90%, nausea 70%, apthous ulcers 30%, oral Candida 20%, blurred vision 2/10, diabetes mellitus 10%, brown spots 10%, migraine 10%.
Shiffman, 2004	Discontinuation of medication: 0.3% PEG-IFN alone, 7% ribavirin alone, 3% both medications. Most common AEs leading to dose reduction or discontinuation: hematologic abnormalities, neuropsychiatric events, fatigue, flu-like and other nonspecific symptoms. Infections requiring dose reduction of PEG-IFN occurred in 1% of patients.	Dose reduction required: 15% PEG-IFN, 18% ribavirin, 21% both medications.

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Sulkowski, 2002	2 withdrawals due to AEs (convulsions and respiratory failure; retinal hemorrhage).	Dose reductions of either PEG-IFN or ribavirin in 6 patients (30%). Specific AEs: myalgia 85%, fatigue 75%, pyrexia 75%, headache 70%, dermatitis 50%, insomnia 45%, rigors 40%, anxiety 35%, nausea 35%, vomiting 35%, anorexia 30%, cough 30%, pruritis 30%, concentration impairment 25%, depression 25%, injection site inflammation 25%, sinusitis 25%, alopecia 20%, appetite decreased 20%, upper abdominal pain 20%, diarrhea 15%, dizziness 15%, dyspnea 15%, nasal congestion 15%, sore throat 15%, weight decreased 15%.
Vere, 2005	Not reported	Adverse events reported in 21 cases (56.72%): hematologic abnormalities (7 cases, 18.9%), fatigue (5 cases, 13.5%), headache (4 cases, 10.5%), myalgia (2 cases, 5.4%), depression (2 cases, 5.4%), and alopecia (1 case, 2.7%). Hematological abnormalities were anemia (1 case, 2.7%), neutropenia (5 cases, 13.5%), and thrombocytopenia (1 case, 2.7%). During therapy, hemoglobin levels decreased within the first 24 weeks with a mean maximal decrease of approximately 3 g/dl, but only in one case was dose reduction necessary. Hematological abnormalities required dose reduction.
Studies of p		

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Bagheri, 2004	8/51(15.7%)	455 adverse drug reactions reported. Most common were influenza-like symptoms (98%) and asthenia. 58% had GI adverse reactions including diarrhea, constipation, epigastralgia, or loss of appetite. 56% had hematologic adverse reactions. Mean weight loss 4.5 kg (SD 3.0, range 2-18 kg). 44% had musculoskeletal AEs including cramps, myalgia, and dorsalgia. 42% had respiratory AEs including cough, dyspnea, and throat irritation. 38% difficulty in concentration, 18% depression, 12% dizziness, 32% irritability, anxiety, or sleeping disorders. One suicide. 32% injection site reactions, 24% urticaria, 4% photosensitivity, 2% facial flush. 22% disturbances in taste, vision, hearing, or smell.
Ballesteros, 2004	28.6% discontinued prematurely: 1 in first week, 1 hemolytic anemia, 1 neutropenia, 1 sepsis without neutropenia, 1 peripheral neuropathy, 3 psychiatric disorders.	Not reported
Cacoub, 2005	No discontinuations	1 (11%) dose reduction, 1 each leukopenia, thrombocytopenia, depression.

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Carnicer, 2005	Treatment discontinuation in 5%	Dose reduction in 18%. Specific AEs: irritation at injection site 82%, flu-like illness, asthenia, myalgia 81%, personality changes 40%, weight loss 40%, anemia, neutropenia, thrombocytopenia 28%, dyspepsia, diarrhea, abdominal pain 25%, depression 20%, cough 17%, pruritus 12%, alopecia 10%, hypothyroidism 4%, pneumonia 2%, chest pain 2%, diabetes mellitus 2%, impotence 2%, bleeding gums 2%, other side effects 10%.
Chang, 2005	Early treatment discontinuation in 53 patients.	Genotype 1: 25 due to failure to respond. Other reasons: depression (n=10), non-compliance (8), anemia or leucopenia (6), and alcohol relapse (1). Genotypes 2 and 3: 3 premature discontinuations (1 depression, 1 non-compliance, 1 severe skin rash).
Dalgard, 2004	Treatment stopped early in 6% of patients,	Dose of PEG-IFN, RBV, or both, was reduced in 20%. Reasons for early treatment cessation or reduction of dose were neutropenia (n=10), anemia (4), depression (3), fatigue (3), diabetes mellitus (1), and other side effects (10). Specific AEs (14 week treatment group, 24-week treatment group): fatigue (48%, 40%), nausea (20%, 8%), depression (22%, 20%), irritability (28%, 28%), alopecia (21%, 24%), influenza-like symptoms (65%, 52%), itching (30%, 12%), exanthema (17%, 8%), anemia (8%, 4%), neutropenia (10%, 4%).
Dan, 2006 US	Not reported	Measured depression, quality of life, and anemia: Average SF-36 scores were lower during treatment than at baseline and after treatment. Vitality, physical function, and social functioning scores were significantly lower during treatment. Anemia and depression were both associated with quality of life impairment.

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Farel, 2004	Not reported	Measured ocular changes 8/23 patients developed ophthalmologic pathology: cotton wool spots (n=7), unilateral cataract (n=1), bilateral cataract (n=1), decrease in color vision (n=2; 19% and 50% decrease, respectively).
Gilleece, 2005	Discontinuation of all treatment due to AEs: (n=1),	Discontinuation due to rising HCV RNA (4). Adverse events (no dose modification required): anemia (n=1), neutropenia (13), depression (16), fever and rigors (10), insomnia (9), myalgia/arthralgia (6), anxiety (8), fatigue (6), dry skin (3), diarrhea (2), nausea (1), mouth ulcers (1), pain at injection site (1), metallic taste (1), nosebleeds (1), shortness of breath (1).
Glesby, 2005	1 withdrawal due to anemia, 1 due to difficulty tolerating peginterferon and ribavirin.	(Grade 1=mild, 2=moderate, 3=severe, 4=potentially life-threatening) 18 subjects reported a grade 2 or higher sign or symptom; 3 reported a grade 3 or 4 sign or symptom. 14 developed a grade 2 or higher laboratory toxicity, and 7 developed a grade 3 or 4 toxicity. Grade 3 AEs were fatigue/malaise (n=2), neutropenia (n=2), ache/pain (n=1), diarrhea/loose stools (n=1), and nausea/vomiting (n=1). Grade 4 AEs were neutropenia (n=3), anemia (n=1), and hyperglycemia (n=1).
Hasan, 2004	3 patients withdrew due to severe flu-like symptoms.	5 patients missed 1 to 3 doses of PEG-IFN. Dose of PEG-IFN was reduced to 1 µg/kg/week in 4 patients (6%). Specific adverse events: flu-like symptoms 79%, weight loss (>10%) 38%, hair loss 45%, anemia 30%, itching 16%, depression 15%, hypothyroidism 6%, discontinuation 4%.

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Kraus, 2005	Not reported	Measured psychiatric side effects. HADS depression scores increased significantly during treatment and returned to baseline level after termination of antiviral therapy. Hostility also increased during treatment. No differences according to mode of therapy (pegylated vs non-pegylated interferon). Dose reduction due to weight loss or intolerability in 14.6% of non-pegylated and 14% of peginterferon group.
Marrache, 2005	Treatment discontinued in 18.7%. Causes of treatment discontinuation: asthenia (n=9), depression (1), irritability, insomnia, headaches (1), patient's decision (1), neutropenia (1), spontaneous bacterial infection (1), increase in ALT (1).	1 serious AE (spontaneous bacterial peritonitis). Dose reduction of PEG-IFN in 8.8% due to neutropenia (n=6), and thrombocytopenia (1).

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Mauss, 2004	Discontinuation due to AEs or treatment failure did not differ between methadone and control groups. Methadone group: 4 patients discontinued due to AEs (weight loss, impaired renal clearance, anemia, alcohol abuse). Control group: 2 patients discontinued due to AEs (hypothyroidism, first manifestation of multiple sclerosis).	At baseline, 6% of patients were treated with antidepressants. During therapy, 25% of patients were treated with antidepressants at any time. At the end of followup, 7% of patients were still on antidepressants. No increase in median daily methadone dose during treatment (55 mg/day vs 50 mg/day); 24 weeks post-therapy, median methadone dose was lower compared to baseline (20 mg/day vs 55 mg/day, p=0.008).
Mazzaro, 2005	One patient interrupted treatment after 13 weeks for depression.	Dose reduction of PEG-IFN required for 2 patients. Quality of life (EORTC QLC-C30 instrument) showed significant improvement between 24 and 48 weeks in global health status and physical functioning, with a worsening of emotional functioning, mainly for depression. No significant changes in cognitive, social, and role functioning. Improvement of fatigue was observed.

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Moreno Planas, 2005	1 treatment discontinuation due to cachexia.	All patients had AEs. Most commonly reported were asthenia (n=11), weight loss (11), fever (9), anorexia (8), rash (7), nausea and/or vomiting (6). Infectious complications occurred and resolved in 3 patients (1 pneumonia, 1 perineal abscess, and 1 cutaneous cellulitis. Most common hematologic events were leukopenia (n=12), thrombocytopenia (11), and anemia (9). Seven of 11 patients who completed therapy required dose reduction (63.6%). PEG-IFN dose reduced in 4 patients due to leukopenia, and RBV dose in 5 due to anemia.
Moreno, 2004	20% discontinued; 17.1% discontinued due to AEs. AEs leading to discontinuation: weight loss >10 kg, lactic acidosis, depression, severe flu-like syndrome, anemia requiring hospitalization and blood transfusion, both depression and flu-like syndrome.	Most frequently reported AEs: flu-like symptoms (97%), skin AEs (69%), GI symptoms (34%), irritability (40%), depression (9%), peripheral neuropathy (9%), weight loss >10% (17%), lactic acidosis (6%)

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Moreno, 2005	11% discontinued treatment due to AEs: (5 HIV infected, 6 HCV monoinfected, 2 liver transplant patients). 8 withdrew between weeks 4 and 24, and 5 before week 48 despite VR at week 24 (4 HCV monoinfected and 1 HIV coinfected). No treatment withdrawals among liver transplant patients after week 24.	No PEG-IFN dose modifications or withdrawals in first 4 weeks. Dose adjustments: HCV mono-infected (8.5%), HIV-coinfected (19%), and liver transplant patients (18%).
Muir, 2004	Blacks vs non-Hispanic whites: Discontinuation: 19% vs 21%;	Rates of AEs, dose reduction, and discontinuation of treatment similar for blacks and non-Hispanic whites. Blacks vs non-Hispanic whites: Dose reduction: 22% vs 24%.

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Myers, 2004	47% withdrew prematurely due to AEs. Psychiatric complications were the most common reason for discontinuation (19%). Reasons for withdrawal: depression (n=3, 1 requiring hospitalization), agitation and delirium (2), anxiety (1), hepatocellular carcinoma (n=1), and non-specific symptoms including fatigue, insomnia, and weight loss (6).	Dose reduction of PEG-IFN required in 16%; neutropenia (n=3), anemia (2).
Perez-Olmeda, 2003	No discontinuations due to anemia. 2 patients lost 8 kg in 6 months (therapy discontinued).	5.5% required dose reduction due to decline in hemoglobin more than 2g/dl. Body weight declined on average 4.6 kg from baseline in patients who completed therapy.

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Raison, 2005	Not reported by treatment group, 11/162 overall (6.8%)	Measured depression: Depression (Zung self-rating depression scale) scores were significantly elevated over baseline by week 4 of treatment and remained increased through the 24th week. 38.9% of patients exhibited moderate to severe depression on at least 1 assessment. Only ribavirin dose significantly predicted the development of moderate to severe depression when baseline depression score was controlled for.
Santin, 2006	Discontinuation of one or 2 of the drugs in 16.7%.	95% had AEs, serious AEs in 16.7%. Dose reduction needed in 11.7%, and Overall AEs: flu-like symptoms 76.6%; weight loss 36.6%; psychiatric disorders 30%; hematological alterations 36.6%; respiratory symptoms 6.6%; dermatological alterations 23.3% Grade III or IV (serious) events: flu-like symptoms 5%; psychiatric disorders 5%; hematological alterations 5%; respiratory symptoms 1.6% Cause of treatment discontinuation: flu-like symptoms 3.3%; psychiatric disorders 6.7%; hematological alterations 3.3%; respiratory symptoms 1.7%; dermatological alterations 1.7%
Seow, 2005	1 patient stopped treatment prematurely after 24 weeks due to excessive lethargy.	Specific AEs: anemia 66.7%, leukopenia 69.7%, thrombocytopenia 45.5%, fatigue 54.5%, fever 48.5%, headache 45.5%, rigors 27.3%, weight decrease 15.2%, arthralgia 27.3%, myalgia 42.4%, anorexia 33.3%, diarrhea 9.1%, nausea 27.3%, giddiness 21.2%, alopecia 33.3%, pruritus 18.2%, rash 9.1%.

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Seyam, 2005	Between weeks 12 and 24, 12 patients withdrew due to treatment intolerance and side-effects; not clear how many at earlier time points.	Measured weight loss: 91.2% of patients had lost weight at 4 weeks, 93.7% at 12 weeks, 94.7% at 24 weeks, and 89.65% at 48 weeks. Median weight losses were 2.3% of pretreatment weight at 4 weeks, 4.6% at 12 weeks, 6.3% at 24 weeks, and 8.9% at 52 weeks. 12 weeks after completion of treatment, median weight had increased to 96.4% of pretreatment weight, and by 24 weeks this had increased to 99%.
Taliani, 2006	19.1% withdrew; 51.9% of those by month 3. AEs leading to discontinuation were hematologic abnormalities (n=9), loss of more than 10% of weight (n=2), ictus (n=1), acute salmonellas (n=1), thyroid dysfunction (n=1), intestinal occlusion (n=1), urticaria (n=1), and severe paresthesia (n=1).	Dose reduction of PEG-IFN in 19%. AEs leading to dose reduction were granulocytes and or platelet depletion (21 cases), psychiatric disorders, mainly depression (12 cases), and fever (3 cases).

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Voigt, 2006	30.0% discontinued treatment. Reasons for treatment discontinuation: patient wish 5.7%, non-compliance 1.6%, lost to followup 1.6%, neuropsychiatric disorders 11.5%, hematological abnormalities 1.6%, flu-like syndrome 2.5%, pleuritis 0.8%, hyperlactatemia 0.8%, cholestatic hepatopathy 0.8%, psoriasis 0.8%, unspecified AE 2.4%. 2 deaths (uncertain circumstances, sudden heart death).	Dose reduction or interruption of ribavirin required in 36%. Patients on zidovudine-containing ART regimens underwent ribavirin dose modifications significantly more often than those on zidovudine-free regimens or no ART (58% vs 29%, p<0.05).
Younossi, 2005	12 patients (7%) discontinued due to neuropsychiatric side effects (severe depression, anxiety, etc), 2 (1.2%) with recurrent nosebleeds. Other reasons for discontinuation were severe fatigue, flu-like syndrome, inability to work.	Significant anemia (hemoglobin <10g.dl) in 11%; severe anemia (<8.5 g/dl) in 0.6%. Thrombocytopenia (platelet count <50,000) on 0.6%, no severe thrombocytopenia (<25,000); significant neutropenia (ANC <750) in 11%, severe neutropenia (<500) in 3%.

Evidence Table 6. Adverse events in uncontrolled and observational studies of pegylated interferons for chronic hepatitis C infection

Author, year	Withdrawals due to AEs	Other main adverse events
Zeuzem, 2004	3% discontinued due to AEs; 2 due to depression and one each for asthenia, anemia, asthenia plus anemia, breast cancer, and psoriasis.	Serious AEs in 25 patients (11%). 26% required dose reduction or interruption due to AEs. Anemia (12%), thrombocytopenia (4%), and neutropenia (3%) were most common AEs leading to dose modification.
Zeuzem, 2006	3% discontinued due to adverse events (2 depression, asthenia, anemia, asthenia plus anemia, breast cancer, and psoriasis).	11% had serious adverse events. Considered related to study medication in 19 of 25 patients (depression, asthenia, abdominal pain, fever, anemia, neutropenia, hypocalcemia, pruritus, rash, psoriasis, allergy, thyroiditis, hearing impairment). 26% required dose reduction or interruption due to adverse events. Most common events leading of dose modifications were anemia (12%), thrombocytopenia (4%), and neutropenia (3%).