PDF created May 26, 2017, 4:04 am

var drug_url = "peginterferon-alfa-2b-drug";

Peginterferon alfa-2b *(PegIntron)*

See also
Peginterferon alfa-2a
.

Table of Contents

Drug Summary

Peginterferon alfa-2b has played a central role in the treatment for chronic hepatitis C for more than a decade when it replaced standard interferon alfa as a treatment for hepatitis C. In 2014, peginterferon alfa-2b remains an important component of hepatitis C therapy. The combination of peginterferon alfa plus ribavirin pus sofosbuvir is currently the preferred regimen for patients with genotypes 1 and 4, with peginterferon alfa plus ribavirin pus simeprevir an alternative.
Peginterferon alfa-containing regmens that were previously considered preferred, but are that are no longer recommended as first-line regimens (a) peginterferon alfa plus ribavirin plus either boceprevir or telaprevir for genotype 1, and (b) peginterferon alfa plus ribavirin for genotype 2 or 3. Although peginterferon alfa-2b is expensive, it is signifcantly less expensive than direct acting antiviral agents, particularly sofosbuvir and simeprevir. In addition, enthuasiasm for peginterferon alfa-2b has been hindered by its extensive adverse effects, necessity for weekly injections, and

limited efficacy in certain patient populations, including those patients who are cirrhotic, HIV-coinfected, or who carry the IL28B TT genotype. With the anticipation that numerous direct acting agents will be approved in the next several years, it is likely that peginterferon alfa will become obsolete as the interferon-free combination regimens become available and become recommended for all hepatitis C genotypes.

Class and Mechanism

Peginterferon alfa-2b consists of interferon alfa-2b covalently linked to a 12-kd linear polyethylene glycol (PEG). The biologic activity of peginterferon-alfa-2b derives from its interferon alfa-2b moiety, which impacts both adaptive and innate immune responses against hepatitis C virus. This alpha interferon binds to and activates human type 1 interferon receptors on hepatocytes which activates multiple intracellular signal transduction pathways, culminating in the expression of interferon-stimulated genes that produce an array of antiviral effects, such as blocking viral protein synthesis and inducing viral RNA mutagenesis. Compared with the native interferon alfa-2b, the peginterferon alfa-2b has sustained absorption, delayed clearance, and a prolonged half life.

Manufacturer for United States

Peginterferon alfa-2b (*PegIntron*) (Figure 1) is manufactured in the United States by Schering Corporation, a subsidary of Merck & Co., Inc.

Cost and Medication Access

The wholesale acquisition cost (WAC) for peginterferon alfa-2b is approximately $8,400 for a 12-week supply, $16,800 for a 24-week supply, and $33,600 for a 48-week supply.

Adverse Effects

In most patients, peginterferon alfa-2b causes numerous problematic side effects. In clinical studies, the most common adverse reactions (reported in greater than 40%)were injection site inflammation/reaction, fatigue, headache, rigors, fevers, nausea, myalgia, and anxiety or emotional lability/irritability. In addition, significant hematologic toxicity can occur due to peginterferon alfa-2a, including neutropenia and thrombocytopenia. Patients can develop ophthalmologic disorders and all patients should receive a baseline eye examination and should have a prompt eye examination if they develop ocular symptoms while on therapy. Neuropsychiatric effects such as insomnia, depression, and irritability can also occur. Peginterferon alfa-2b may cause or aggravate life-threatening neuropsychiatric, autoimmune, ischemic, or infectious disorders. Further, the use of peginterferon alfa-2b in patients with cirrhosis can cause life-threatening hepatic decompensation. To report suspected adverse reactions, contact (1) Schering Corporation, a subsidary of Merck & Co., at 1-800-526-4099 or (2) the FDA at 1-800-FDA-1088.

Key Drug Interactions

For complete information on peginterferon alfa-2b-related drug interactions, see the Drug Interactions section in the Peginterferon alfa-2b (*PegIntron*) Prescribing Information.

Clinical Trials

Filter by Category

- All Clinical Trials
- Resistance/Virological Failure
- Resistance/Virological Failure
- Resistance/Virological Failure
- Resistance/Virological Failure
- Resistance/Virological Failure
- Resistance/Virological Failure
- Pharmacology
- Pharmacology

Atlantic Coast Hepatitis Treatment Group: Peginterferon alfa-2b plus Ribavirin in Blacks and Non-Hispanic Whites

In this multicenter study performed in the United States, investigators sought to evaluate the efficacy of peginterferon alfa-2b 1.5 mcg/kg weekly plus ribavirin starting at 1000 mg daily for 12 weeks followed by 800 mg daily among blacks compared with non-Hispanic whites. They reported significantly lower sustained virologic response (SVR) rates among blacks (19%) compared with whites (52%, $p<0.001$); this disparity in SVR rates was explained primarily by race, and not socioeconomic status or genotype. The types and frequency of adverse events were similar in the two groups. This study clearly showed that black patients wiht genotype 1 infection have a lower response to treatment with peginterferon plus ribavirin than non-Hispanic whites.

View Clinical Trial: In your Browser | Download PDF

IDEAL: Peginterferon alfa-2a versus Peginterferon alfa-2b

The IDEAL Study is one of the largest trials of both forms of peginterferon alfa, designed as a head-to-head comparison of the two forms of peginterferon alfa (2a versus 2b) and to also compare two doses of peginterferon alfa-2b. Treatment-naïve patients with genotype 1 infection were randomly assigned to one of three treatment arms: (1) standard-dose (1.5 mcg/kg) peginteferon alfa-2b plus

ribavirin (800-1400 mg/day), (2) low-dose (1 mcg/kg) peginteferon alfa-2b plus ribavirin (800-1400 mg/day), and (3) standard-dose (180 mcg) peginteferon alfa-2a plus ribavirin (1000-1200 mg/day). Patients who had an early virologic response had markedly higher SVR rates than those who do not achieve an early virologic response. The rates of sustained virologic responses and the incidence of adverse effects did not differ substantially across these regimens.

View Clinical Trial: In your Browser | Download PDF

International Hepatitis Interventional Therapy Group: Peginterferon alfa-2b plus Ribavirin versus Interferon alfa-2b plus Ribavirin

This randomized controlled trial is one of the largest to examine peginterferon alfa-2b; it compared two different doses of peginterferon alfa-2b plus ribavirin (1.5 mcg/kg per week plus 800 mg ribavirin versus 1.5 mcg/kg per week for 4 weeks followed by 0.5 mcg/kg per week of peginterferon alfa-2b plus weight-based ribavirin of 1000-1200 mg/day for 48 weeks). These arms were also compared with standard interferon-2b with ribavirin among 1,530 patients with previously untreated chronic hepatitis C (HCV). The sustained virologic response rate was highest among the patients in the higher 1.5 mcg/kg dosing of peginterferon alfa-2b (54%) compared with lower-dose peginterferon alfa-2b (47%, p=0.01) or standard interferon (47%, p=0.01). Most of the benefit in this regimen was observed in those with genotype 1 HCV infection.

View Clinical Trial: In your Browser | Download PDF

Peginterferon alfa-2b plus Ribavirin for 12 or 24 weeks in HCV Genotype 2 or 3

This study is one of the first to examine the efficacy of a response-guided approach to treatment duration, comparing a standard 24-week duration of pegIFN-2b at a dose of 1 mcg/kg weekly plus weight-based ribavirin 1000-1200 mg daily with a “variable-duration” arm that treated at the same doses but allowed patients who achieved HCV viral suppression at week 4 to stop therapy after 12 weeks in treatment-naïve patients with genotype 2 and 3 HCV infection; those patients who failed to suppress completed 24 weeks of therapy. This variable-duration approach appeared to be as effective as the standard duration, achieving sustained virologic response in 77% patients compared to 76% in the standard-duration arm, with lower rates of adverse events and treatment withdrawal.

View Clinical Trial: In your Browser | Download PDF

Peginterferon alfa-2b plus Weight-Based Ribavirin in HCV Genotype 2 or 3

This phase 4 study was a single-arm, open-label trial that assessed the safety and efficacy of 24 weeks of peginterferon alfa-2b 1.5 mcg/kg once weekly plus weight-based ribavirin 800-1400 mg/day in treatment-naïve patients with genotype 2 or 3 HCV infection. A sustained virologic response (SVR) was achieved in 93% of genotype 2 and 79% of genotype 3 patients with this regimen, comparable to the historical SVR rate of 84% with 48 weeks of therapy among genotype 2 and 3 patients. A lower pre-treatment HCV viral level, treatment duration of at least 16 weeks and minimal or no steatosis (less than 5%) were all independent predictors of SVR. Adverse events that required dose reduction or treatment interruption occurred in 18% patients.

View Clinical Trial: In your Browser | Download PDF

RIBAVIC: Peginterferon versus Interferon in HCV-HIV Coinfection

This open-label trial randomized 412 HIV-HCV coinfected patients to either 48 weeks of peginterferon alfa-2b plus 800 mg ribavirin daily versus 48 weeks of standard interferon alfa-2b plus 800 mg RBV. The pegIFN-2b group had a higher rate of sustained virologic response compared with the control arm (27% versus 20%, p=0.047) with most of the benefit seen in patients with genotype 1 or 4. The absolute difference however was smaller than that noted in the peginterferon alfa-2a trials of coinfected patients. Tolerability of these regimens were comparable however the pegIFN-2b arm experienced more dose reductions due to clinical adverse events (16% versus 7%, p=0.004).

View Clinical Trial: In your Browser | Download PDF

WINR Trial: Peginterferon alfa-2b and Weight-Based or Flat-Dose Ribavirin

This very large, prospective, open-label trial enrolled 5207 hepatitis C treatment-naive patients at 236 sites in the United States to examine the impact of weight-based or flat-dose ribavirin given with peginterferon alfa-2b. Patients in the study were randomized on a 1:1 basis to receive peginterferon alfa-2b plus flat-dose ribavirin or peginterferon alfa-2b plus weight-based ribavirin. At the beginning of the trial, all patients were scheduled to recieve 48 weeks of therapy, but the protocol was amended so that patients with genotype 2 or 3 were randomized to receive either 24 or 48 weeks of therapy. Overall, SVR24 rates were higher in patients who received weight based ribavirin compared with flat-dose ribavirin. When analyzing for gentoype 1 patients, those who received weight based ribavirin compared with flat-dose ribavirin (34% versus 29%). WIth genotype 2 and 3 patients, no significant differences were observed with weight-based versus flat-dose ribavirin and extending treatment to 48 weeks did not significantly improve SVR rates. This study demonstrated a benefit of using weight-based ribavirin in combination with peginterferon alfa-2b when treating patients with gentoype 1 HCV, but not with genotype 2 or 3.

View Clinical Trial: In your Browser | Download PDF

References

- Awad T, Thorlund K, Hauser G, Stimac D, Mabrouk M, Gluud C. Peginterferon alpha-2a is associated with higher sustained virological response than peginterferon alfa-2b in chronic hepatitis C: systematic review of randomized trials. Hepatology. 2010; 51:1176-84. [PubMed Abstract]
- Berenguer J, González-García J, López-Aldeguer J, et al. Pegylated interferon {alpha}2a plus ribavirin versus pegylated interferon {alpha}2b plus ribavirin for the treatment of chronic hepatitis C in HIV-infected patients. J Antimicrob Chemother. 2009;63:1256-63. [PubMed Abstract]
- Carrat F, Bani-Sadr F, Pol S, et al. Pegylated interferon alfa-2b vs standard interferon alfa-2b, plus ribavirin, for chronic hepatitis C in HIV-infected patients: a randomized controlled trial. JAMA. 2004;292:2839-48. [PubMed Abstract]
- Jacobson IM, Brown RS Jr, Freilich B, et al. Peginterferon alfa-2b and weight-based or flat-dose ribavirin in chronic hepatitis C patients: a randomized trial. Hepatology. 2007;46:971-81. [PubMed Abstract]
- Mangia A, Santoro R, Minerva N, et al. Peginterferon alfa-2b and ribavirin for 12 vs. 24 weeks in HCV genotype 2 or 3. N Engl J Med. 2005;352:2609-17. [New England Journal of Medicine]
- Mangia A, Thompson AJ, Santoro R, et al. Limited use of interleukin 28B in the setting of response-guided treatment with detailed on-treatment virological monitoring. Hepatology. 2011;54:772-80. [PubMed Abstract]
- Manns MP, McHutchison JG, Gordon SC, et al. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. Lancet. 2001;358:958-65. [PubMed Abstract]
- McHutchison JG, Lawitz EJ, Shiffman ML, et al. Peginterferon alfa-2b or alfa-2a with ribavirin for treatment of hepatitis C infection. N Engl J Med. 2009;361:580-93. [PubMed Abstract]
- Muir AJ, Bornstein JD, Killenberg PG. Peginterferon alfa-2b and ribavirin for the treatment of chronic hepatitis C in blacks and non-Hispanic whites. N Engl J Med. 2004;350:2265-71. [PubMed Abstract]
- Tungol A, Rademacher K, Schafer JA. Formulary management of the protease inhibitors boceprevir and telaprevir for chronic hepatitis C virus. J Manag Care Pharm. 2011;17:685-94. [PubMed Abstract]
- Zeuzem S, Buti M, Ferenci P, et al. Efficacy of 24 weeks treatment with peginterferon alfa-2b plus ribavirin in patients with chronic hepatitis C infected with genotype 1 and low pretreatment viremia. J Hepatol. 2006;44:97-103. [PubMed Abstract]
- Zeuzem S, Hultcrantz R, Bourliere M, et al. Peginterferon alfa-2b plus ribavirin for treatment of chronic hepatitis C in previously untreated patients infected with HCV genotypes 2 or 3. J Hepatol 2004;40:993-9. [PubMed Abstract]

Figures

Figure 1 Packaging - Peginterferon alfa-2b (*PegIntron*)

Photo: Andrew Karpenko, University of Washington

Figure 2 RediPen® - Peginterferon alfa-2b (*PegIntron*)

Photo: Andrew Karpenko, University of Washington

Figure 3 RediPen® Dose Selector - Peginterferon alfa-2b (PegIntron)

Photo: Andrew Karpenko, University of Washington