Interferon Alfacon-1
A Novel Interferon for the Treatment of Chronic Hepatitis C
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Abstract Interferon alfacon-1 (consensus interferon; CIFN) is a novel, recombinant interferon which has been shown to have greater biological activity in vitro than other interferons. CIFN was tested in a large, phase 3, multicentre, North American study in patients with chronic hepatitis C. Patients were treated with 9μg CIFN or 3MU interferon (IFN)-α-2b 3 times weekly for 6 months. Efficacy was assessed by changes in ALT, decrease in hepatitis C virus (HCV) RNA and im-
provement in histology. CIFN produced similar overall response rates to those seen with IFNα-2b. However, the response rate and decrease in HCV RNA were greater among genotype 1 patients treated with CIFN than among those treated with IFNα-2b. Patients with sustained response generally responded early in treatment, with 96% responding by week 12. There was also a better response to CIFN than to IFNα-2b in patients with a high baseline viral concentration. Although the majority of CIFN-treated patients had histological improvement in the liver, it is notable that even patients who relapsed or did not respond had histological improvement and thus benefited from CIFN treatment. Viral and histological benefits were similar in patients with and without cirrhosis although ALT levels were not as improved in those with cirrhosis.

Patients who relapsed or did not respond to initial treatment with either CIFN or IFNα-2b were re-treated with a higher dose of CIFN (15μg). Patients who relapsed had a 58% sustained viral response rate with 12 months of re-treatment. The response to re-treatment with this regimen of CIFN monotherapy is similar to that reported with the standard combination regimen of IFNα-2b plus ribavirin and far superior to that observed with 3MU IFNα-2b alone. Although prior non-responders had a lower response rate than relapsers (sustained viral response rate of 13%), it is nonetheless clinically meaningful and clearly superior to the negligible responses among nonresponders reported in previous studies using re-treatment with other interferons.

The adverse effects noted with CIFN are similar to those reported for IFNα-2b and are recognised adverse effects for all interferons. Thus, CIFN is a unique interferon with enhanced antiviral activity. Providing greater benefit for the difficult-to-treat patients makes CIFN a beneficial alternative in the initial treatment and re-treatment of patients with chronic hepatitis C.

Interferon alfacon-1 (consensus interferon; CIFN) is a novel interferon with enhanced in vitro biological activity compared to other interferons. CIFN is marketed under the trade names of Infergen® and Inferax®. Clinically, CIFN has proven to be an effective initial treatment for chronic hepatitis C and is effective in the re-treatment of patients who have either not responded or relapsed after initial interferon treatment. This article attempts to outline some of the unique features of CIFN from a preclinical and clinical perspective.

1. Preclinical Information

1.1 Design of Interferon Alfacon-1

Interferon was first recognised for its ability to interfere with viral replication.[1] Although antiviral activity is still a dominant feature of interferons, we now recognise that interferons have many biological activities in vitro including antiproliferative activity, natural killer cell activation, immune modulation, histocompatibility antigen induction, etc.[2] Interferons are also part of a complex web of cytokines in vivo. Although interferons have been used successfully in many clinical indications, their mechanism of action for any indication is not precisely known. One can only speculate on the relationship between observed in vitro activity and clinical activity. The clinical efficacy observed with interferons may be due to a single biological function, a combination of biological activities or to interactions with other cytokines and mediators.

Although interferon-β (IFNβ) and interferon-γ (IFNγ) are each derived from single genes which give rise to single proteins, interferon-α (IFNα) is a family of proteins.[2] There are 20 to 25 species of IFNα which differ in their amino acid sequence and/or glycosylation. These species of IFNα also differ widely in their biological activities.[3] Species that are potent in one particular activity in vitro...