
... SELECTED ABSTRACTS ...

The following abstracts, from peer-reviewed journals containing literature on hepatitis and its medical management, were selected for their relevance to this supplement.

Interferon Treatment Decreased Liver Fibrosis Without ALT Normalization

A study was conducted to assess the progressions per year of liver fibrosis and activity in patients treated for 6 months with 3 MIU of interferon (IFN) and to compare these progressions between i) treated patients, ii) treated patients with normalization of ALT at 3 months, and iii) control patients never treated with repeated biopsies before the utilization of IFN. One hundred and sixty-eight patients with hepatitis C were included. The liver fibrosis and activities were staged according to the METAVIR score. Results showed a significant reduction of the annual progressions of liver fibrosis and activity in the treated group (0.02 and -0.12, respectively), compared with the control group (0.30 and 0.17, respectively). In the treated patients with normalization of ALT at 3 months, the reduction of annual progression of liver fibrosis was significantly higher compared with the control group (-0.07, $P < 0.001$). In the treated patients with normalization of ALT at 3 months, the reduction of annual progression of activity (-0.54) was significantly higher ($P < 0.001$) compared with the control group and the treated group. IFN treatment for 6 months' duration decreased the annual progression of liver fibrosis and activity even without normalization of ALT at 3 months.

Mathurin P, Thevenot T, Sobewski R, et al. Six months with interferon alpha (IFN) decreased the progression of liver fibrosis and activity in patients with chronic hepatitis C without normalization of ALT at 3 months (NR-3M). *Hepatology* 1996;24:157A. Abstract 122

Comparison Between 6 and 12 Months Interferon (IFN) Therapy in Patients With Undetectable Serum HCV RNA After 1 Month of Treatment

Two different durations of IFN therapy (6 and 12 months) were compared in patients with undetectable serum HCV RNA after 1 month. One hundred and thirty patients affected by biopsy-proven chronic hepatitis C were treated with IFN administered at different doses related to body weight and HCV genotype (5-8 MIU TIW for Type 1, 3-5 MIU TIW for all others). Fifty-eight patients with normal ALT and undetectable serum HCV RNA after 1 month of therapy were randomized to complete 6 or 12 months of therapy. The maintenance of normal ALT and negative HCV RNA 6 months after the end of treatment was considered as a sustained response. Results of 48/58 patients (83%) with undetectable serum HCV RNA after 1 month who completed 6 or 12 months of therapy showed that 12-month treatment is significantly ($P < 0.01$) more effective than 6-month therapy (sustained response rate was 77.8% and 26.7%, respectively). Overall, results suggest that in patients with undetectable serum HCV RNA after 1 month of therapy, 12-month treatment is significantly more effective than 6-month therapy.

Bellobuono A, Tempini S, Vicari F, Chiodo F, Idéo G. Comparison between 6 and 12 month alpha interferon therapy in patients with undetectable serum HCV RNA after 1 month of treatment in chronic hepatitis C. *Gastroenterology* 1997;112:A1225. Abstract

Alfa Interferon Prevents Hepatocellular Carcinoma in Responders

Three subgroups of patients with hepatitis C-associated cirrhosis, long-term responders (previously treated with IFN), nonresponders (previously treated with IFN), and controls, were compared based on the incidence of hepatocellular carcinoma (HCC). Patients were followed for 41 to 57 months to determine changes during this period. Results indicated a global decrease in the incidence of HCC with IFN treatment (treated vs control $P < 0.02$) with a highly significant difference between long-term responders and controls ($P < 0.008$) and a significant difference between nonresponders and controls ($P = 0.005$). A significant difference was not shown between long-term responders and nonresponders. This study showed that IFN treatment reduced the risk of HCC development in long-term responders with HCV-associated cirrhosis.

Accogli E, Mazzella G, Sottili S, et al. Alfa interferon prevents hepatocellular carcinoma in responders with HCV-associated hepatic cirrhosis. *Gastroenterology* 1997;112:A1206. Abstract.

Prolonged Course Versus 6 Months of Interferon or No Treatment

The incremental cost effectiveness of prolonged interferon (IFN) treatment versus a standard 6-month course or no treatment in patients with histologically mild chronic hepatitis C was estimated using a decision-analysis model. A Markov model of the natural history of chronic hepatitis C was used to project lifetime clinical and economics outcomes. Results suggested that 36.4% of patients with mild chronic hepatitis C normalized serum ALT and remained viral-negative (sustained response) after 18 to 24 months of IFN vs 15.3% for 6 months and no response without treatment. Based on these responses, cost and outcome were projected for hypothetical cohorts. Cost of IFN and medical care, IFN response rate, and rate of disease progression were significant variables in sensitivity analyses. This analysis suggests that treatment with 18 to 24 months of IFN in patients with mild chronic hepatitis C should further prolong life expectancy as compared to a 6-month course or no treatment. With increasing age (>35 years), there was a decrease in life gained, and the cost of each of those years increased progressively. Overall, the analysis showed that a gain in life expectancy in patients younger than 70 years is achieved at a reasonable marginal cost-effectiveness ratio.

Davis GL, Beck JR, Farrell G, Poynard T. Prolonged course versus 6-months of interferon alfa or no treatment in patients with histologically mild chronic hepatitis C: A decision analysis. *Gastroenterology* 1997;112:A1252 Abstract

Histological Response of Interferon Therapy in Chronic Hepatitis

The histological response of interferon (IFN) therapy in nonresponders and long-term responders was studied in 110 patients who were serum HCV antibody-positive and histologically diagnosed with chronic active hepatitis (CAH). Liver biopsies were taken before and after treatment to determine the degree of inflammation and fibrosis between the sustained responders and nonresponders. It was shown that intrahepatic fibrosis was further advanced in 26% of the nonresponders and modified in only 7% 3 years after treatment, while it was modified in 25% of the sustained responders. Fibrosis was further advanced in about 50% of 10 untreated patients with HCV genotype 1b after 3 or more years. The inflammatory reaction was modified by IFN in 50% of even the nonresponders. Overall results suggest that IFN therapy may slow the progression of liver disease by modifying the intrahepatic inflammatory reaction irrespective of its therapeutic effect.

Segawa T, Moriyama M, Shibahara N, et al. Histological response of interferon therapy in chronic hepatitis C. *Gastroenterology* 1997;112:A1378 Abstract

HCV-RNA As a Predictor of Relapse After Interferon Therapy

Eighty patients with chronic hepatitis C enrolled in an open study were treated with IFN at a dose range of 3 to 6 MIU TIW for 12 months. ALT levels were monitored monthly, and HCV RNA was evaluated at the first, third, and sixth month during therapy. IFN was stopped if a complete response was not achieved within 6 months. A sustained response, defined as persistent normalization of ALT during follow-up, was achieved in 28 of 43 patients who achieved a complete response. The results showed that a sustained response is predicted in 100% of cases by undetectable HCV RNA levels at the first and third month of IFN therapy. In contrast, relapse can be expected when HCV RNA is positive both at the third and sixth month of therapy. HCV RNA monitoring is a reliable method to predict treatment response during IFN therapy and design cost-effective therapeutic strategies.

Colloredo G, Bellati G, Ricci A, et al. HCV-RNA as a predictor of relapse after interferon therapy for chronic hepatitis C. *Hepatology* 1996;24:156A Abstract 117.