Media Release

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Pegasys combination provides "considerable clinical advantage" over interferon alfa-2b and ribavirin in treatment of hepatitis C, New England Journal of Medicine reports

The combination of Pegasys - a new generation pegylated interferon for the treatment of hepatitis C - and ribavirin "provides a considerable clinical advantage" over interferon alfa-2b and ribavirin", says a new study published today in the New England Journal of Medicine. Interferon alfa-2b plus ribavirin has been the leading prescribed hepatitis C therapy in the United States since it was introduced.

The aim of the randomized, controlled clinical trial conducted in 81 centers worldwide, was to determine if Pegasys (peginterferon alfa-2a (40 KD)) plus ribavirin is more effective than interferon alfa-2b plus ribavirin or Pegasys monotherapy in the treatment of chronic hepatitis C, a blood-borne liver disease affecting more than 170 million people worldwide.

The authors noted that Pegasys plus ribavirin significantly enhanced the sustained virological responses (defined as undetectable virus) regardless of viral genotype or viral load when compared to interferon alfa-2b plus ribavirin. More specifically the study reports:

- "Significantly higher" overall sustained viral response of 56% compared to 44% with interferon alfa-2b plus ribavirin
- For patients considered to have the most difficult-to-treat disease, genotype 1 and high viral levels, there was a substantial increase in sustained virological response of 41% versus 33%
- Patients with cirrhosis had an increased sustained virological response of 43% compared to 33% with interferon alfa-2b plus ribavirin

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- Patients with genotypes 2/3 obtained a sustained virological response of 76% versus 61% with interferon alfa-2b plus ribavirin.

"This was the first large multi-center trial comparing Pegasys plus ribavirin to interferon alfa-2b plus ribavirin, and the study results indicate that this new combination offers patients a better chance of being cured," said lead author, Dr. Michael Fried, Associate Professor of Medicine and Director of Clinical Hepatology at the University of North Carolina at Chapel Hill.

Less flu-like symptoms and depression

The overall safety profiles of the three treatment regimens were similar. However, the study found that side effects typically associated with the use of interferons (including flu-like symptoms and depression) were reported less frequently with Pegasys combination therapy relative to interferon alfa-2b plus ribavirin.

The authors noted that this "is a particularly important observation demonstrating that superior efficacy can indeed be achieved with peginterferon alfa-2a plus ribavirin without commensurate increases in those adverse events most commonly associated with interferon-based therapies."

Predicting Treatment Outcome

By week 12 (of a 48-week course of treatment), a vast majority (86%) of patients treated with the Pegasys combination had achieved an early virological response. An early response was indicative of achieving a sustained response, which occurred with the majority (65%) of patients. In contrast, the few patients who did not achieve an early response, were unlikely to achieve a sustained response.

"Early prediction of virological response is a valuable tool for physicians," said Dr. Fried. "It can help identify who is likely to succeed with this treatment. Importantly, it can also help clinicians to determine whether to discontinue therapy for those not responding, saving patients the side effects and cost of additional therapy," he said. Dr. Fried cautioned that this must be considered on an individual patient basis.

Leadership in Hepatitis C Research

Today's article is the third Pegasys clinical study that the NEJM has published during the last two years and the first pegylated interferon to be published in this prestigious journal. It marks the 9th original article to be published on Pegasys clinical data, and reflects Roche's comprehensive research program, which includes participation from nearly 20,000 patients.

About Pegasys

Pegasys, a new generation hepatitis C therapy that is different by design, provides significant benefit over conventional interferon therapy in patients infected with HCV of all genotypes. The benefits of Pegasys are derived from its new generation large 40 kilodalton branched-chain polyethylene glycol (PEG) construction, which allows for true seven-day viral suppression and is preferentially distributed to the liver, the primary site of infection. Pegasys is administered once weekly in an easy-to-use formulation with a fixed 180 mcg starting dose for all patient types.

Pegasys has been approved in 47 countries, including the European Union. Pegasys has also been submitted for review by regulatory authorities in the United States and Roche expects approval in monotherapy and combination later this year.

About Hepatitis C

Hepatitis C is a serious blood-borne viral infection that attacks the liver, and in many patients it leads to liver disease, cirrhosis and cancer. It is the leading cause of liver transplantation. Only identified in 1989, the HCV virus has infected more than 170 million people world-wide, making it more common than the HIV virus.

About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-orientated healthcare groups. The company's two core businesses in pharmaceuticals and diagnostics provide innovative products and services, that address prevention, diagnosis and treatment of diseases, thus enhancing people's health and quality of life. The two core businesses achieved a turnover of 13,1 billion Swiss Francs in the 1st half of 2002 and employed about 57'000 employees worldwide.

Roche is committed to the viral hepatitis disease area, having introduced Roferon-A for hepatitis C, followed by Pegasys in hepatitis C. Pegasys is also in phase III clinical development for patients infected with the HBV virus. Roche also manufactures The COBAS AMPLICOR™ HCV Test, v2.0 and the AMPLICOR HCV MONITOR™ Test, v2.0 - two tests used to detect the presence of, and quantify, HCV RNA in a person's blood. Roche's commitment to hepatitis has been further reinforced by the in-licensing of Levovirin, an alternative antiviral. Levovirin will be studied with the objective of demonstrating superior tolerability over the current standard, ribavirin.

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Notes to the editor:

- Sustained virological response or SVR is the criterion for assessing the efficacy of a hepatitis C medication and it indicates that there is no detectable virus in the blood 24 weeks (six months) after completion of therapy.
- The ribavirin used in conjunction with PEGASYS in the present study is Roche's new ribavirin, COPEGUS®.
- The 1,121 patients participating in this study came from: Australia, Austria, Belgium, Brazil, Denmark, Finland, France, Germany, Greece, Italy, Mexico, The Netherlands, Norway, Portugal, Spain, Switzerland, Taiwan and the USA.

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* Study Design section of Fried paper notes that medications included once-weekly injections of 180mcg peginterferon alfa-2a (PEGASYS, F. Hoffmann-La Roche Ltd.), plus ribavirin (F. Hoffmann-La Roche) or thrice-weekly injections of 3 MIU (million international units) of interferon alfa-2b plus ribavirin (Rebetron™), Schering-Plough Corporation.

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