

EASL: Interferon Lambda as Effective as Alfa for Hepatitis C but with Much Better Safety Profile

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A new form of pegylated interferon, interferon lambda, is associated with significantly fewer side effects than the standard form of the drug, interferon alfa, in a study conducted in patients with easier to treat hepatitis C genotypes 2 and 3, researchers reported at the 47th International Liver Congress (EASL 2012) in Barcelona.

Data from the EMERGE Phase 2b study demonstrated that pegylated interferon lambda was as effective as pegylated interferon alfa. The major advantage of the new compound was that it caused significantly fewer side effects. Interferon lambda or alfa was taken in combination with ribavirin. Another key finding of the study was that there were fewer dose reductions of both interferon and ribavirin with the lambda-based combination.

A number of drugs which work directly against hepatitis C have been approved or are in development. However, for the foreseeable future these will need to be taken in combination with pegylated interferon and ribavirin. The side effects associated with these two drugs are a major limitation of hepatitis C therapy. Therefore a more tolerable form of interferon would be advantageous in order to allow more patients to start and complete therapy and to achieve a cure.

Preliminary research has shown that pegylated interferon lambda is as effective as interferon alfa but has a benign side effect profile when used for the treatment of hepatitis C genotype 1. Investigators conducted further research to assess the efficacy and tolerability of this new form of pegylated interferon in patients with genotypes 2/3.

A total of 118 treatment-naive patients were recruited to the study. Therapy lasted for 24 weeks. Treatment responses up to 24 weeks post completion of treatment were assessed. An undetectable hepatitis C viral load at week 24 was defined as a sustained virological response.

None of the patients had cirrhosis and they were randomized in equal proportions into four treatment arms. Individuals in three of the arms were treated with a weekly dose of pegylated interferon lambda (120, 180 or 240 mcg) plus ribavirin. Patients in the fourth arm received pegylated interferon-alpha and ribavirin and served as controls.

There were no significant baseline differences between the treatment arms.

Rates of sustained virological response for the lambda-treated patients ranged between 57% and 83%. The best results were seen for the 180 mcg dose (genotype 2 = 71%; genotype 3 =

83%). These compared to a response rate of between 40% and 67% for patients in the control arm.

In most respects interferon lambda had a superior safety profile to interferon-alpha. An interferon dose reduction was necessary for between 7% and 13% of the lambda patients (180 mcg = 7%) compared to 27% of those treated with interferon alfa.

None of the patients taking the lambda formulation needed to reduce their dose of ribavirin because of low hemoglobin. However, a ribavirin dose reduction was necessary for 23% of the patients taking interferon-alpha.

Flu-like symptoms developed in between 17% and 23% of those treated with interferon-lambda. This compared to a rate of 40% for patients in the control arm.

Musculoskeletal symptoms also occurred less frequently in the lambda-treated patients than in those treated with interferon-alpha (17%-28% vs 63%).

Fatigue was reported by 50% of patients treated with the 240 mcg dose of lambda, by 28% of those on the 180 mcg dose and by 41% of individuals in the 120 mcg arm. This compared to a prevalence of 53% among the alpha-treated patients.

Overall, approximately 9% of patients in the lambda study arms developed anemia, compared to a prevalence of 45% in the control arm. None of the patients treated with lambda developed either neutropenia or a low platelet count. This compared to rates of 52% and 24% respectively in the alfa-treated patients.

ALT or AST elevations five or more times higher than the upper limit of normal developed in 3% of patients treated with the 240 mcg lambda dose. None of the other lambda doses were associated with these abnormalities in liver function, and this was also the case for interferon-alpha. Elevated bilirubin was seen in 7% of patients treated with the highest lambda dose. None of the other lambda doses or interferon alfa caused this disturbance.

In some other respects the safety profiles of lambda and alpha interferon were similar. Most notably both drugs were equally likely to cause neuropsychiatric side effects (lambda prevalence 40%-45% vs 33% alfa).

A press release issued by the manufacturer Bristol-Myers Squibb stated that the results suggested that lambda had the potential to meet unmet needs of hepatitis C-infected patients and that the data supported further investigation of the compound.

S Zeuzem, S Arora, B Bacon, et al. Peginterferon lambda-1-a (Lambda) compared to peginterferon alfa-2a (alpha) in treatment-naïve patients with HCV genotypes (G) 2 or 3: first SVR24 results from Emerge phase IIB. 47th Annual Meeting of the European Association for the Study of the Liver (EASL 2012). Barcelona, April 18-22, 2012. Abstract 10.