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Biostatistician Review Report

Title of the Manuscript: Pegylated interferon alpha-2b plus ribavirin therapy in treatment of chronic hepatitis C

I have reviewed the Statistical analysis of the data for the above cited study as requested by the authors. The following are the comments of the above study:

Methodology:

Sample size required for this multicenter study was computed based on the following: Various trials conducted on genotype 1&4 or 2&3 patients have reported around 40-80% SVR, which reflects the efficacy of peginterferon alfa-2b in the treatment of hepatitis C virus.^[1,2] In the earlier pilot study conducted on 25 patients with HCV infection, 60% SVR was observed. Therefore, considering 60% of efficacy, 95% CI, 80% power and 15% error with 15% dropout rate with two tailed t-test, the calculated sample size was 100 patients.

Since open-label, single arm study design was adopted, efficacy assessment upon basically relied descriptive statistics. Intention-to-treat (ITT) analysis was carried out on the population that included all patients who met the eligibility criteria and had received at least one dose of investigational drug during the study period.

The primary efficacy endpoint was percentage of patients achieving sustained virologic response and secondary endpoints were percentage of patients



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achieving rapid virologic response, early virologic response, end of treatment virologic response and normalization of alanine aminotransferase. Safety parameters such as vital signs were analyzed by repeated measurements, and laboratory findings, which include hematology (prothrombin time, hemoglobin, complete blood picture, platelet count) and biochemical parameters (liver function tests, renal function tests, random blood glucose, serum electrolytes, thyroid function tests), were analyzed by repeated measure analysis of variance. All p-values reported were two-sided and p-values less than 0.05 were considered statistically significant. All analysis were done using IBM SPSS version 19.0 for Windows. All the above review comments are correct to the best of my knowledge.

References:

1. **McHutchison JG**, Manns M, Patel K, Poynard T, Lindsay KL, Trepo C, Dienstag J, Lee WM, Mak C, Garaud JJ, Albrecht JK. Adherence to combination therapy enhances sustained response in genotype-1-infected patients with chronic hepatitis C. *Gastroenterology* 2002; **123**: 1061-9 [PMID: 12360468 DOI: 10.1053/gast.2002.35950].
2. **Manns MP**, McHutchison JG, Gordon SC, Rustgi VK, Shiffman M, Reindollar R, Goodman ZD, Koury K, Ling M, Albrecht JK 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**: 958-965. [PMID: 11583749 DOI:10.1016/S0140-6736(01)06102-5]


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