Reviewer's report

**Title:** Studies on best positive predictors for sustained virologic response to interferon alpha plus ribavirin therapy in Naive Chronic Hepatitis C Patients

**Version:** 2 **Date:** 12 July 2008

**Reviewer:** Gloria Taliani

**Reviewer's report:**

Major comments:
In the present study a really good rate of SVR (51.56%) is reported in HCV patients treated with non-pegylated IFN and ribavirin. Although this result may depend on racial and/or virological characteristics of the study population, it is quite different from the results reported in other populations treated with the same schedule and IFN type. To this high response rate could, at least in part, contribute the exclusion of some patients from the analysis. In fact, on page 9 we find the following sentence: “Out of these 400 patients, 280 were males and 120 females. Six patients (four males and two females) discontinued treatment due to severe side effect of treatment at month 2 and were excluded from data analysis”. This is not correct because these patients have received the treatment for 2 months and should be computed as non-responders on intention to treat analysis. Thus, SVR rate should be recalculated after inclusion of these patients and the result should be correctly reported in all the sections of the manuscript, including the abstract. In addition, although the PCR method employed in the present study has a quite low sensitivity (100 copies/ml of HCV-RNA) which may contribute to misclassify partial responders with low residual HCV-RNA titer as end treatment responders, the relapse rate after therapy withdrawal is surprisingly low (16%), and this is an unexpected result which deserves some comments and some clarification from the authors.

Table 2, which reports the results of the analysis of virological response at week 8, end of treatment and end of follow up, is difficult to understand. I made the calculation myself with either Fisher’s exact test and Chi square test and found no significant difference between males and females in any type of virological response. Thus I wonder which test has been applied for the calculation of such a significant difference reported by the Authors. Besides, I did not find any difference between males and females by Chi Square test and Fisher’s exact test based on the data reported in table 5. Thus, a revision of the statistical analysis is strongly advised.

The definition of Rapid Virological Response (RVR) given by the Authors is not correct. By definition, the RVR is the negative HCV-RNA by week 4 of therapy and not by week 8 as indicated by the Authors. The wrong definition should be corrected along all the manuscript.

The number of patients who had a liver biopsy examination is really low (57 patients) compared to the cohort of treated patients (400 patients) and this...
makes impossible to infer data about the response rate of different ethnic groups (Pashtoon versus Punjab), of cirrhotic patients or make a multivariate analysis concerning the predictors of response. In addition, no data about the compliance of the patients to the therapy are reported, which introduces a further uncertainty about the reliability of the predictors of response.

In Table 3, the groups of patients divided according to the infecting genotype are too many and some groups include less than 5 patients, which is useless: genotypes may be grouped in 1 and non-1. This last group can be sub-divided in genotype 2 and 3. Finally, it could be interesting to examine in deeper detail those patients with mixed genotypes who did not respond to the treatment in order to evaluate which genotype was the resistant one.

Also Table 4 is too detailed. A ROC of age and response could be done to determine the best age cut-point and age analysis should be done according to it.

Finally, the discussion is too long. It should be shortened and focused on really relevant points regarding data correctly re-analyzed. The manuscript should undergo a careful revision by an English mother tongue reviewer.

Minor Comments:

In the text it is reported that some examined factors are “…..independent risk factors for low SVR”…. Which is not correct. These factors are independent PREDICTORS OF NON RESPONSE. The concept of “low response” is not applicable to HCV treatment: there is only the possibility of “response” or “non response”.

In the abstract, the following sentence should be reworded ” the patients data collected prospectively was at this Centre from 2001 to 2007 was analyzed”.

On page 7, the following sentence should be reworded “Further the patients were required to negative for hepatitis B surface antigen…”

On page 7, the following sentence should be reworded “Patients were excluded from the studies that were <18 years or above 70 years.”

Tables should be carefully revised because of typing errors (e.g. Table 1, the percentage of genotype 3 females is not 18.78) or mistakes (Table 2 P values; Table 5 sex P value).

Many other misspelling, grammar and syntax errors are present in the manuscript and should be corrected.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

No competing interests exist