Reviewer's report

Title: Interleukin-22 predicts severity and death in advanced liver cirrhosis: A prospective cohort study

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Reviewer: Ashwani Singal

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Kroenberger et al have addressed role of IL-22 in predicting survival in cirrhotics and concluded that elevated levels of IL-22 > 18 predict poor survival. Although, the idea is novel but I have major concerns and criticisms before accepting this biomarker for utility in clinical practice:

1. Background: Poorly developed and does not stretch to specific aims of the paper. For example authors themselves rightly point out protective role of IL-22 and fail to provide sufficient background information on which the study hypothesis is based

2. Methods: a) It is not clear whether elevated levels of IL-22 are taken at the baseline or any time during the follow up, b) not clear how the survival was recorded as many patients would die outside the hospital, and c) did no one drop out of the study and this seems really surprising for me especially for sick patients as included in this study

3. Results: a) Tables and figures are redundant. For example figure 2 and 5 could be combined into one figure and figure 7 and 8 may not be needed, b) results of cox regression analysis are not provided on which the whole conclusion is based, and c) as IL-22 could be marker for regeneration was any attempt made to correlate this with levels of AFP another established marker of liver regeneration

4. Discussion: a) The significance of the study is not convincing. Is it possible that high levels are just a reflection of severity of liver disease ? Does IL-22 clear through the liver and what is its pharmacokinetics ? b) It would have been better if authors looked at the c-statics of IL-22 and compared to established prognostic model MELD score. Pearson calculation may not be the right way to look at as IL-22 has not been shown by the authors as a continuous score in this study like MELD score. Rather prognostic value of IL-22 was shown at a cut off of 18.

In addition language is tardy at many places. For example Blood sampling heading should be replaced with collection of blood samples, decompensated liver disease heading in table 1 should be liver related complications, liver disease heading in table 1 should be etiology of liver disease, cell death heading in table 2 should be liver enzymes to name a few !

Quality of written English: Not suitable for publication unless extensively edited
Statistical review: Yes, and I have assessed the statistics in my report.