Reviewer's report

Title: Interleukin-28B gene non-TT allele strongly predicts treatment failure for genotype 1 infected chronic hepatitis C patients with advanced fibrosis: a case control study

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Reviewer: Chia-Yen Dai

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Hu et al. conducted their study enrolling 42 biopsy proven hepatitis C virus (HCV) patients with advanced fibrosis (Ishak fibrosis score, #4) and 126 sex- and HCV genotype-matched patients without advanced fibrosis (Ishak fibrosis score, #3) to determine the impact of IL-28B genetic variants on the treatment efficacy of CHC patients receiving peg-IFN/RBV for 24 weeks. Authors concluded that in HCV genotype 1 infected advanced fibrosis, patients with IL28B rs8099917 genotype TT, achieving RVR had similar SVR rate with those without advanced fibrosis. And patients with non-TT genotype without achieving RVR are suggested to stop therapy. Generally speaking, the issue seems important in countries where DAA are not yet easily available.

Major Compulsory Revisions:

1. The major concern of the present study is the treatment regimen was suboptimal that HCV-1 patients received peg-IFN/RBV therapy for only 24 weeks. As most of the studies implicated that patients with genotype 1 have to receive 48 weeks therapy in standard. For patients with RVR and low viral load may receive shortened course.

2. The pretreatment viral load deserves clearer description. To analyze the known important determinant RVR+viral load for the better response in the study is critical. Authors used 800,000 IU/ML as cutoff of the low and high viral load. It is also interesting to explore the cutoff of RNA level for predicting SVR in patients with or without advance fibrosis. What is the condition when RVR, IL 28B SNP and viral load are considered together?

3. In the present study 44.4% of SVR rate was observed from HCV GT1-infected group A patients with an RVR. The viral load has to be taken into consideration firstly. By the way, the 44.4% SVR rate is lower than previous randomized control studies in Taiwan (76~89% for patients with GT1 and RVR). Authors may explain the possible reasons. How about the SVR rate from HCV GT1-infected group B patients with an RVR?

4. Page 17 line 295: In this study, authors found that none of the patients with advanced fibrosis and rs8099917 non-TT genotype achieved an RVR, and all of them failed to have an SVR after 24 week therapy. What are the roles of viral load and cEVR in these patients?

Minor Essential Revisions:
5. Page 13 line 227: lower HCV RNA should be “pretreatment lower HCV RNA level”

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'