Reviewer's report

Title: Simeprevir with pegylated interferon alfa 2a plus ribavirin for treatment of hepatitis C virus genotype 1 in patients with HIV: a historical comparison

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Reviewer: Charitha Gowda

Reviewer's report:

- Review of Statistics

The authors attempt to investigate a clinically significant research question – specifically, to evaluate the efficacy of simeprevir+PegIFN#+RBV vs PegIFN#+RBV alone in HIV-1/HCV-coinfected patients. While the study’s methodology and statistics are sound, the use of a “non-adjusted indirect comparison” study design limits the strength of the authors’ findings and should be more clearly highlighted as a major limitation of this study. This is particularly significant given the substantial heterogeneity in the studies included in the meta-analysis, as noted by the authors.

The authors do address study heterogeneity in part by using random effects modelling; however, they did not pursue additional testing or investigation of the underlying causes of the observed heterogeneity in order to provide a more concrete context for interpretation of study findings. The authors briefly mention this as a potential limitation for their study design and described how sensitivity analyses were performed which supported their main analyses. However, only limited sensitivity analyses were performed – i.e. repeating analyses among trials that had same treatment duration or weight-adapted RBV dose as study C212. Other potentially important confounders that should have been investigated include proportion of patients with cirrhosis included in the studies (which was quite variable, ranging from 10 to 51% in the trials included) and proportion of treatment-experienced vs treatment-naïve patients (not available for most trials included). This article would be strengthened by providing more details on characteristics of the studies included and their patient populations: e.g. data on trial design (i.e. blinding/concealment, visit frequency, drop-out procedure), trial setting (geography, multicenter, etc), and other patient characteristics (i.e. baseline disease severity, control of HIV infection, HAART regimen used). By providing more information on how similar/dissimilar the patient populations were, this would at least allow readers to interpret the potential extent and direction of bias present.

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

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.