Author’s response to reviews

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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We thank the reviewers for their time and effort spent to review our paper.

Reviewer No. 2 raised the point that the historical comparison presented in the manuscript may not have clinical impact, as the results from randomized controlled trials with newer DAAs performed in HCV-monoinfected individuals may be extrapolated to those with HCV/HIV coinfection. We agree with the reviewer that available data from RCTs indeed indicate that for the newer DAAs, there may no difference in absolute treatment response rates in patients with HCV monoinfection and HCV/HIV coinfection and already discuss that in the discussion section of the manuscript (line 289-291).

However, a systematic formal analysis (e.g. a meta regression analysis of all available trials) supporting extrapolation of results from RCTs that excluded patients with HCV/HIV coinfection is not available so far, to the best of our knowledge. In addition, even if the outlined position is generally accepted within the scientific community, regulatory authorities and national institutions deciding about the reimbursement status of drugs may have a more formalistic view on this aspect (i.e. may request formal evidence in the patient population of HIV/HCV coinfected patients instead of relying on the assumption that results from trials that excluded that patient population can be extrapolated).

Finally, if one is interested in the relative treatment effect of Simeprevir+IFNalfa+ribavirin vs. IFNalfa+ribavirin alone (e.g. to address comparative efficacy or to estimate numbers needed to treat), results from RCTs that excluded patients with HCV/HIV coinfection cannot be easily extrapolated to patients with HCV/HIV coinfection. It is known that the response to IFNalfa+ribavirin (i.e. the control group) is lower in patients with HCV/HIV coinfection. If the response rate with Simeprevir+IFNalfa+ribavirin is similar in patients with and without coinfection (SVR24 of approx. 70%-80%), while the response rate with IFNalfa+ribavirin is lower in patients with coinfection, extrapolating the results from trials in patients with monoinfection would tend to
underestimate the true relative difference of Simeprevir+IFNalfa+ribavirin vs. IFNalfa+ribavirin in patients with HCV/HIV coinfection. We are thus still convinced that the presented historical comparison is of scientific and clinical relevance.