The British Association for the Study of the Liver (BASL) and the British Viral Hepatitis Group (BVHG) welcome NICE's review of Sofosbuvir/Ledipasvir.

We agree with their summaries on the use of these agents in non-cirrhotic GT1 and GT4 patients, and for GT1 and GT4 treatment-naïve cirrhotic patients. We believe that the clinical data, and the cost-effectiveness data presented in the ACD, support the use of Sofosbuvir/Ledipasvir for 8 weeks in GT1 naïve non-cirrhotic patients, and for 12 weeks in GT1 and GT4 treatment-experienced non-cirrhotic, and treatment-naïve cirrhotic patients.

Where we have concerns is in the analysis of GT1 and GT4 treatment-experienced cirrhotic patients. NICE have assessed the cost-effectiveness based on a 24 week regimen, whilst we believe that the assessment should be made on a 12 week regimen (where trial data has suggested very good efficacy – including ION-2, the post-hoc analysis of Bourliere presented at AASLD 2014 (abstract O82), and the recent SIRIUS study published online http://dx.doi.org/10.1016/S1473-3099(15)70050-2 and comment http://dx.doi.org/10.1016/S1473-3099(15)70094-0, which suggests that a 12 week regimen with ribavirin provides 95% SVR in patients with Childs A cirrhosis including prior non-responders to a protease inhibitor).

We understand that this position has been taken as a result of the wording of the marketing authorisation, but we disagree with the stated interpretation. Our view is that these patients treated with Sofosbuvir/Ledipasvir do have re-treatment options in the event of not attaining an SVR – especially as genotypic and phenotypic resistance to Sofosbuvir in vivo is exceedingly rare, and therefore Sofosbuvir could be re-utilised in combination with another DAA class, (e.g. protease inhibitor) or interferon. Furthermore we believe that the vast majority of GT1 and GT4 treatment-experienced cirrhotic patients in the UK have a low risk of short to medium-term clinical progression, especially those with Child-Pugh scores below 7 and no previous decompensation.

We believe that a 12 week regimen of Sofosbuvir/Ledipasvir in GT1 and GT4 treatment-experienced cirrhotic patients is therefore clinically valid, and likely to be cost-effective, and would be our preferred option in such patients.

The other patient group we would like to highlight to the committee are those with GT3 who are interferon-intolerant or ineligible. These patients have relatively few treatment options at present. Some good efficacy has been shown for 12 weeks of Sofosbuvir/Ledipasvir in naïve non-cirrhotic patients (as demonstrated in ELECTRON-2 (Gane et al., EASL 2014)) . There is a clinical need for better and alternative therapies in those with cirrhosis as the only presently NICE-approved therapy would be 24 weeks Sofosbuvir & Ribavirin. Thus it will be important for NICE to consider the combination of Sofosbuvir plus Daclatasvir, or possibly Sofosbuvir/Ledipasvir (Ledispavir is less potent in vitro than Daclatasvir against GT3 and we await the results in vivo). We appreciate that it may not be possible for NICE to consider data that becomes available once the ACD is in process but we view this patient group as being in high clinical need.

Many thanks for permitting us to comment.