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Meindert Boysen
Programme Director, Centre for Health Technology Evaluation
Submitted via NICE Docs

From [redacted]

11 June 2015

Dear Mr Boysen

Re: NHS England response to the Appraisal Consultation Documents for Hepatitis C Drug Appraisals

The Royal College of Physicians (RCP) plays a leading role in the delivery of high quality patient care by setting standards of medical practice and promoting clinical excellence. We provide physicians in the United Kingdom and overseas with education, training and support throughout their careers. As an independent body representing over 31,000 fellows and members worldwide, we advise and work with government, the public, patients and other professions to improve health and healthcare.

The RCP is grateful for the opportunity to respond to comments received from NHS England with regards to the following treatments for hepatitis C:

- ledipasvir-sofosbuvir [ID742]
- daclatasvir [ID766]
- ombitasvir/paritaprevir/ritonavir with or without dasabuvir [ID731]

We support almost all of the arguments made by the BSG/BASL/BHVG/RCPath in their joint submission as well as those made by our own Joint Specialty Committee for Genito-urinary Medicine (see below for further details). We also acknowledge the difficulties in introducing new and very effective treatments which are expensive in a cash-constrained NHS. It is vital that NHS England, NICE and the profession collaborate to ensure that such treatments are introduced in a way that does not compromise care either for that patient group or at the expense of other patient groups.

The detailed arguments and evidence base is made in the other responses mentioned above, and our position can be summarised as:

- We believe the evidence for cost effectiveness for these new treatments is clear and that later additional data than that available in NHS England's submission increases the cost effectiveness of these new therapies compared with their calculations. This evidence is significant and robust.
- We support NICE guidelines and outcome monitoring as opposed to Multiple Technology Appraisals for these treatments.
- We believe a 'watch-and-wait' approach is unproven and likely to endanger patients as well as creating large additional costs. The new treatments are affordable if introduced in a measured roll-out agreed with the clinical community and patients. It is clear from the specialty society responses that the profession is fully engaged with such a process.

- We support NICE and it is important that implementation of NICE recommendations is done in a consistent way rather than on a case-by-case basis

Response from the Joint Specialty Committee for Genito-urinary Medicine

We are grateful for the opportunity to respond to comments received from NHS England with regards to Sofosbuvir/ledipasvir, daclatasvir and parateprávir/ritonavir, ombitasvir and dasabuvir for the treatment of HCV.

Whilst we appreciate the financial constraints that NHS England is currently under, we are not in agreement with the comments made to NICE with regards to the publication (and the implementation, thereafter) of the above technology assessments.

There are a number of specific issues we want to bring to the NICE committee's attention in this regard

1) We would like to point out that whilst the Viral Hepatitis group of the Infectious Diseases CRG were consulted on the NHS England response there clearly was not agreement from all the members of this clinical group in supporting the NHS England comments (as apparent in the covering e-mail.) As representatives of associations representing patients and clinicians/health-care professionals looking after patients with HIV/HVC co-infection, we too disagree with some of the assertions made by NHS England.

2) We would question NHS England's assertion that there are uncertainties in treatment effects and comparative effectiveness

    a) NHS England state the the 'evidence base is small particularly in more severe patients (ie patients with cirrhosis)' – as the Committee are no doubt aware, there have been a number of real-life cohorts (including the NHS England EAP in de-compensated cirrhotics) and phase 3 (Solar-1 study) that have presented/published data on the effectiveness of IFN-free DAAs in cirrhotics including de-compensated cirrhotics. Further data will not change this.

    b) NHS England also state that 'there is lack of evidence in harder to reach populations (eg co-infection with HIV) – there are now data from large phase 3 studies and cohort studies, that put beyond any reasonable doubt (ION-4, ALLY-3, Trio, ANRS cohorts) that DAA-based therapies perform just as well in co-infected patients. Furthermore, as NHS England are well aware, more than 80% of patients with HIV-infection in the UK are already in care and the vast majority have their hepatitis status diagnosed (with regular screening) and are linked into care for their viral hepatitis (see BHIVA National Audit 2010).

3) NHS England question the static nature of the cost-effectiveness models stating re-infection and onwards transmission as sources of uncertainty. We would like to highlight that a number of modelling studies, including work from the UK (N Martin, et al EASL 2015) have taken into account the impact of re-infections on cost-effectiveness of testing and treatment. Similarly, in the context of HIV-infection, modelling studies based on the UK CHIC data have also shown that reducing the burden of disease and new HCV infections amongst HIV+ MSM will require treatment with DAA-based therapy for >80% within a year of diagnosis and 20% of chronically-infected per annum (N Martin, et al EASL 2015). We are not convinced that further data will change these assertions and that time is now right to try and reduce burden of disease in these vulnerable, high-risk populations.

4) The omission of relevant treatment strategies: watchful waiting and treatment sequences. We would like to highlight to the Committee that 'watchful waiting and monitoring for disease progression' has a cost associated with it, and whilst this may be possible for the current patients in care, this will have

significant resource-use implications for the future. Furthermore, such a strategy may be detrimental in the case of rapid progression in some groups (eg sub-groups of HIV co-infected patients). We would also like to point out that HCV-infection is a chronic inflammatory condition and has effects outside of the liver (renal disease, bone disease, cardiovascular disease, poor psychological health, fatigue) and that this may be particularly more pronounced in co-infected patients (see Wormack, et al. J Am Heart Assoc, 2014; 3e:001035, Molnar, et al. Hepatology 2014, Geisbrecht, et al. Plos One 2014; 9:e89556).

We are also disturbed that given therapies with significantly fewer side-effects (and better SVR rates) that NHS England would even consider sequencing therapies, with 'less expensive' PegIFN and ribavirin (+/- first generation PIs): this is clearly counter-intuitive in terms of patient (and clinician) acceptability

5) Opportunity costs of high-cost medications affecting large populations. We would highlight that whilst there is a large population with HCV infection in England, the vast majority remain undiagnosed (28500 diagnosed of an estimated 160 000 known to be infected), and of those diagnosed not necessarily all are under regular follow-up and 'in care'. It is therefore highly unlikely that uptake of treatment according to NICE guidance will have the suggested impact on NHS England budget in a single year but that even if treatment is taken up by all known to services this would be over a period of many years.

6) Capacity constraints. We, and others have highlighted that the infra-structure and capacity to deliver DAA-based therapy had already been established by NHS England for the delivery of the EAS for de-compensated cirrhotics. An expansion of the number of networks delivering DAA-based care is already underway and that for co-infected patients networks of care have been established. Further refinement of delivery can happen in parallel to establishing therapy, a further delay will not be helpful.

7) NHS England state that 'all stakeholders who have advised NHS England have indicated the importance of forming a multiple technology appraisal…' We were certainly not consulted in this regard and believe that with the fast evolving therapeutic landscape of HCV therapy an MTA would not be possible for a few years to come and would take a further 1-2 years to complete. As NICE and NHS England are both well aware this is not feasible for all therapy areas (HIV treatment, for example) and would unnecessarily delay implementation of therapy for groups of patients that would not meet NHS England's 'priority' group.

8) Prioritisation strategies. Whilst we applaud the NHS England DAA EAS for de-compensated cirrhotics, we are concerned that there are already significant delays in delivering DAAs to the compensated cirrhotics (this programme was initially promised in May 2015 and has yet to be implemented). We would point out that the strategy of 'watchful waiting' is also associated with a cost to the NHS and a burden on already full clinics. Furthermore, this would be detrimental to the sub-group of patients with rapidly progressing liver disease (a significant sub-group of HIV/HCV co-infected patients, for example) and patients who default regular follow-up creating inequalities in healthcare delivery for certain sub-groups of society (homeless, migrant communities, PWIDs, for example).

9) We are also concerned that 'prioritisation' strategies will be liver disease-based (as already implied in the NHS England response) and will disadvantage certain populations with significant HCV morbidities that are not necessarily associated with significant liver fibrosis. As we have already pointed out, there is a significant association between extra-hepatic morbidities associated with HCV and successful treatment, certainly in HIV-infected patients of even those with milder fibrosis (<F2) is associated with significantly improved overall survival (Berenguer et al, JAIDS 2014; 66: 280-7). In fact national/international guidelines (AASLD, EASL guidelines 2015) recognise this and recommend prioritising treatment for certain sub-groups without significant fibrosis.

10) We remain unconvinced that the 'recommendation with research' position that NHS England urges for those without cirrhosis will deliver therapy to those most in need of DAA-based therapy. We believe

that ‘further research’ in this area is best delivered by robust data-collection, as therapy is rolled-out as per guidance.

In conclusion, we would urge NICE to move forward with its recommendations and for NHS England to engage fully with all stakeholders (including national organisations, patient advocacy groups) so that DAA-based treatment can be delivered efficiently and equitably. We would strongly recommend the use of evidence-based clinical guidelines to guide use of particular DAAs in sub-groups of patients.

Yours sincerely

Dr