

Brian Cooper notes:

- In the list of authors, change David Mutimer to Prof.
- There are two instances of Table 8.2, and text call-outs to it.

Gary Brook:

On page 93 the guidelines talk about HEV being faeco-orally spread through contaminated water, which is the case in the developing world. In the UK and Europe many/most cases are probably related to pork consumption. e.g De Silva et al Unexpectedly high incidence of indigenous acute hepatitis E within South Hampshire: time for routine testing?. Journal of Medical Virology, 2008;80:283-8

David Rowlands from BASELINE Magazine sent the following message:

Great to see these guidelines moving forward.

Would it be possible to include ways in which we can work with patients to reduce re infection after treatment?

Also printed resources, tools and media formats for patients starting treatment. staying on treatment and after treatment support.

And a strong input into Decision making within their care

Emma Page:

Dear Brian & Ed

I have a chage to make..... to my acute Hepatitis C section:

1) Page 81, 8.10.3, last sentence paragraph 1. Please change to
Recent data from EuroSIDA continue to show a year-on-year increase in HIV-positive MSM, with an incidence of greater than **1.5** per 100 person-years in 2010 [105].

Best wishes, Emma Page

Kaveh Manavi:

I have only read the summary section of the new guidelines. This is a really helpful document. I particularly like the auditable outcomes sections.

I would like to make two comments on the guidelines:

1. HDV screening of patients with chronic HBV infection: To the best of my knowledge, this is of clinical value when the patient has liver failure, or undetectable HBV VL without being on treatment. How can this screening impact on the management of those on truvada, with undetectable HBV viral load, and with no evidence of fibrosis on TE? I quickly browsed the HDV section of the guideline, and could not find the answer. Also, what can be done in

those on truvada with undetectable HBV VL and detectable HDV viral load? I don't think this is quite clear either.

2. TE measurements: The guidelines are very helpful with the frequency of fibrosis monitoring of those with liver fibrosis. What should be the frequency of screening for those with no evidence of liver fibrosis please? Apologies if I have missed this point if already mentioned.

Kind regards
Kaveh

William Tong:

For the hepatitis Delta section 7, one of the references cited (no 4, Toby et al) was an abstract. The full paper is now published. I think we should replace the abstract with the paper, which is

Tong CYW, Asher R, Toby M, et al. A re-assessment of the epidemiology and patient characteristics of hepatitis D virus infection in inner city London. J Infect. 2013;**66**:521-7.

The percentage of hepatitis Delta co-infection in this full paper is 6% and the figure quoted in the text should reflect this. i.e.

"In the UK, the reported prevalence of HDV among HBsAg-positive patients ranges from 2.1 to 8.5% [1–3] and in those with HBV/HIV infection from 2.6 to 6% [2,4,5], which is lower than the prevalence of 14.5% reported from a European HIV cohort [6]. "

Regards

William

Paul Grime from Faculty of Occupational Medicine sent the following message:

Thank you for including the Faculty of Occupational Medicine in this consultation. The guidelines appear very thorough and comprehensive. Apart from one reference to occupational acquisition of HCV, there is nothing else about occupational exposure and transmission of HIV and hepatitis viruses, or about HIV (co) infected healthcare workers (or other workers), but perhaps that is outside the scope of the guidelines as outlined in the purpose and scope. However, (ii) preventive measures and immunisation could be relevant to HIV infected healthcare workers, although perhaps not more so than other HIV infected patients.

David Bell from NHS Greater Glasgow and Clyde sent the following message:

I am an ID Consultant also working some time in the virology lab.

My main comments relate to the lab implications of the guidelines.

There is no mention of the role of Hepatitis C antigen testing in this guideline. We are using this in Glasgow in place of HCV PCR in some circumstances - particularly screening of patients

with risk factors for infection. The test is in use in many other centres and should be included.

4.2.1.9. Is Occult HBV sufficiently common in HIV infected patients to justify the use of HBV DNA in all sAg negative patients with raised ALTs? Are you suggesting there will be a high rate of occult HBV in sAg negative and core AB negative patients? A significant proportion of HIV patients will have ALTs > 30/19 and require this test. I can see the utility of HBV DNA in patients who are sAg negative and core positive. I suggest that you change this statement to say test DNA in core positive patients only.

6.2.43 - recommends HBV genotyping prior to PEG. The NICE HBV treatment guideline is due out in June 2013 and this will say that genotype should not be used to guide choice of therapy - PEG vs. Nucs.

Thanks

David Bell

Dr Patrick Cadigan, registrar from Royal College of Physicians (RCP) sent the following message:

The RCP is grateful for the opportunity to comment on the consultation. We have liaised with the Joint Specialty Committee for GUM and would like to return the following comments.

Summary recommendations

Section 4.4.1 immunisation and recommendations

HAV vaccination: recommendation 26 to vaccinate all HIV+ against HAV differs from BHIVA immunisation guidelines (which recommend vaccinating those at risk of HAV or its complications only, ie not all HIV-positive per se) – will the immunisation guidelines be updated accordingly? Should the website include a note that where recommendations differ between guidelines the most recent guideline should be used? Does the guideline need to note that the advice differs from the older immunisation guidelines and therefore supersedes it? The new guidance would mean vaccinating far more individuals than we do currently.

HBV vaccination:

- What about missed doses?
- What is the minimum and maximum interval between doses?
- Recommendation 31 advises sAb every 2 years if sAb titre >100; again differs from BHIVA Immunisation guidelines. Comments apply as per recommendation 26
- Recommendation 32 advises HBV booster if sAb <10; immunisation guidelines advise if <10 and ideally if <100 – comments as per recommendation 26
- Vaccination – note the shift away from rapid protocols which have become very popular in sexual health clinics this would benefit with some additional highlighting.

HBV screening:

- Ongoing screening for HBsAg even if vaccinated (4.4.1.33) – this is a bit easier from an order set point of view but is likely to have a very low yield in a vaccinated population. Is this really

justified? Again labs might be a bit concerned at the number of tests heading their way.

Section 6

Occult HBV

Guidelines need to be more explicit that isolated core Ab can be associated with occult HBV

Section 7.1.1

HDV:

- Recommendation 65 only repeat HDV testing in those with HBV is risk factors. Should that include all IDU and, if from an endemic country, only those that continue to visit that country? What about HIV/HBV co-infected individuals who have sexual partners from an endemic country?
- HDV screening of patients with chronic HBV infection: To the best of our knowledge, this is of clinical value when the patient has liver failure, or undetectable HBV VL without being on treatment. How can this screening impact on the management of those on truvada, with undetectable HBV viral load, and with no evidence of fibrosis on TE? In quickly browsing the HDV section of the guideline, we could not find the answer. Also, what can be done in those on truvada with undetectable HBV VL and detectable HDV viral load? We believe this could be made clearer.

Full sections

Section 6

HBV treatment:

- Algorithm 1 p51
 - o Presumably box should read ‘and, not ‘an’
 - o Please clarify ‘AN’ and ‘OR’ – needs to be clearer please
- Algorithm 2 p52
 - o Please clarify what it meant by “HIV resistance to 3TC/FTC and/or tenfovir HBV”
- As we understand the guideline recommends that entecavir can be used where tenfovir is contraindicated. It is important to note that entecavir has renal toxicity as well. We believe that this needs more clarification whether dose adjustment of entecavir or close monitoring for renal function would be needed or not if entecavir is used in patients with impaired renal function

10.1.1 Frequency of HCC screening

- Criteria for HCC screening – now include all Hep B which we would support on a anecdotal basis having had two HCCs in co-infected HIV-hep B pts with suppressed HBV and no cirrhosis (10.1.1.126)
- Given for cirrhotic patients but not for non-cirrhotic individuals with HIV and HBV – is that 6 or 12 monthly?
- DO HCV patients without cirrhosis need regular USS? Please clarify

Frequency of fibrosis assessment

TE measurements: The guidelines are very helpful with the frequency of fibrosis monitoring of those with liver fibrosis. What should be the frequency of screening for those with no evidence of liver fibrosis please?

HCV

- HCV as such is associated with increased risk of insulin resistance in general population and the risk has been found to be more in HIV coinfecting patients. That means HIV-Hep-C coinfecting patients remain at higher risk of developing diabetes and monitoring or screening for diabetes may be relatively more important in this group of patients
- We are not fully convinced by epidemiological data linking cocaine use to Hep C in terms of a population incidence of all cocaine users being examined and not sure that it is practical to attempt to divide your cohort into regular cocaine users or not: it is very hard to audit guidance such as this and difficult to operationalise in practical terms when pts are arriving for their blood check visits a week ahead of their annual review. We would prefer to see a briefer guidance on HCV testing frequency that is more operationally robust.
- Chapter 5 choice of therapy: We feel there wasn't a clear answer to the rhetorical question posed – We think the answer comes eventually at 8.5.1 (could be linked?). : One key question was identified by the Writing Group: when deciding ART for adults with HCV/HIV infection, is there a preferred combination which differs from those with HIV mono-infection
- Role of HCV Ag testing is not mentioned (we are adopting this in Glasgow as first line HCV screening test in HIV patients instead of PCR
- (multiple places, includes 4.2.1.12, 15, 8.3.1.68).

Unexplained transaminitis:

Cut off for ALT has been lowered below many standard lab cutoffs (6.3.1.45), at least in the terms of discussion of HBV therapy.

In 4.2.1.9 and 4.2.1.16 it is advised to exclude HBV with DNA test and HEV with PCR (9.1.120) in this situation or at least the guidelines might be taken that way

Same again for HCV PCR in any MSM with a 'raised ALT' without the caveat of excluding common causes first. (page 63, table) but the definition of abnormal ALT is not given.

Have the lab implications been considered? Just trying to work through the typical results sign off scenarios to translate these guidelines into what to do with an ALT of 39

For HEV exclusion is to be done 'when other causes have been excluded' but couldn't that be said for all the other rare causes of transaminitis? Perhaps it would help to illustrate a typical/agreed plan for investigation of unexplained transaminitiits?

Alastair Miller from Royal Liverpool University Hospital sent the following message:

I think these guidelines are really excellent and much much better than any European and US equivalent. They offer really good practical advice with a fantastic literature review. My only slight quibble is with recommendation 90 - I think this is too strongly worded against treatment and ignores some of the practical problems about availability of future antivirals. At present, we have relatively good availability of PIs (BOC/TPV) for Rx of GT1 but it is totally unclear about how new DAAs will become available either through NICE or CCGs so my feeling is that these guidelines should be less discouraging of treating people now with triple therapy. I am also quite surprised that there is nothing on triple therapy for acute HCV - I know that data is sparse but it

is certainly being sued in the US and probably should at least be considered.

Thanks for an excellent piece of work

Daisy Ellis from Terrence Higgins Trust sent the following message:

1. Terrence Higgins Trust response to BHIVA consultation on BHIVA guidelines for the management of coinfection with HIV-1 and hepatitis viruses.

1.1 Terrence Higgins Trust is the UK's largest HIV and sexual health charity, with 31 service centres across the UK. We are a campaigning and membership organisation which advocates on behalf of people living with or affected by HIV or poor sexual health.

1.2 We provide services for people living with HIV to manage their condition and access emotional and practical support. These include one-to-one counselling, peer support groups, health trainers and information and advice covering benefits, housing, finances, employment and immigration. We also deliver community based clinical services, such as chlamydia screening and rapid HIV testing, and health promotion campaigns and initiatives which target populations most at risk of HIV and poor sexual health.

1.3 Terrence Higgins Trust welcomes the opportunity to respond to this consultation on the BHIVA guidelines for the management of coinfection with HIV-1 and hepatitis viruses. We regard these guidelines as comprehensive and fully support their implementation.

1.4 We would recommend that the guidelines should also include a specific recommendation that individuals should be made aware of local services and organisations or, where these may not exist, national services for additional support. We would strongly advise that each HIV clinic provides information of the local voluntary and support services available to individuals so they can seek further help if they wish..

1.5 Additionally, we would welcome the production of a shorter, user friendly version. Whilst we acknowledge that the guidelines are aimed at "clinical professionals involved in and responsible for the care of adults with HIV and viral hepatitis coinfection, and at community advocates responsible for promoting the best interests and care of adults with coinfection"; we would advocate that guidelines are accessible to all. We would welcome a simplified version that we can share on our website to give people essential information to help them participate in decisions relating to their care.

1.6 For further information please contact Daisy Ellis, Head of Parliamentary and Policy,

Dr Matthew Dryden from British Society for Antimicrobial Chemotherapy sent the following message:

Thank you for giving the BSAC the opportunity to consider the new British HIV Association guidelines for the management of co-infection with HIV-1 and hepatitis viruses 2013. The BSAC members have seen the guidelines and are satisfied with its content. Whilst we have no specific

comments on this occasion we would be very pleased to be included in any future consultations.

With regards

Matthew Dryden, General Secretary, BSAC

Abid Shah from RCOG sent the following message:

Thank you for giving us an opportunity to comment on this guideline. The guideline does not specifically cover pregnancy or women and so we have nothing further to add. We co-developed a guideline on HIV in pregnancy with BHIVA in which there is a specific section on hepatitis and HIV co-infection.

Alan Smith from Gilead Sciences sent the following message:

Dear Guidelines team,

Congratulations on an extremely useful set of co-infection treatment guidelines. We welcome the guidelines and also the structured format.

We would like to comment on the following sections.

1.2.6 Guideline updates and date of next review

We request further clarity regarding the commitment to update the guidelines again in 2015 and to publish amendments and addendums as important data are presented. A number of new molecules with positive impact for co-infected patients will potentially become available before 2015. As stakeholders we would find a clearer outline of processes and timelines helpful.

8.5.1 Choice of ART

The document explores the use of boceprevir and telaprevir with certain anti-retroviral agents. We have 2 comments on this section.

Firstly, although Table 8.2 outlines that rilpivirine can be used without dose adjustment this is not reflected in the recommendations section 8.5.1. Eviplera, offers a single tablet regimen which is generally well tolerated and we feel is an important option for patients. Would an additional bullet point reflecting this be appropriate along with the 2 current bullet points (below)?

- We recommend if boceprevir is to be used, raltegravir (RAL) with tenofovir (TDF) plus emtricitabine (FTC) should be the treatment of choice for those with wild-type HIV (1C).
- We recommend if telaprevir is to be used either RAL or standard-dose ritonavir-boosted atazanavir should be used: efavirenz may be used but the telaprevir dose needs to be increased to 1125 mg tds (1C).

Pharmacokinetic interaction between etravirine or rilpivirine and telaprevir in healthy volunteers: a randomised, two-way crossover trial. Kakuda T, Leopold L, Nijs S, et al. 13th International Workshop on Clinical Pharmacology of HIV Therapy, Barcelona, April 2012, abstract O_18.

Absence of a significant pharmacokinetic interaction between the hepatitis C virus protease

inhibitor boceprevir and HIV-1 NNRTI rilpivirine. Rhee E, et al. 19th Conference on Retroviruses and Opportunistic Infections, March 2013, Abstract 537.

Secondly, Table 8.2 does not look mention Stribild or the Elvitegravir/ Cobicistat components. As there is no currently published data would it be possible to include Elvitegravir/ Cobicistat in the table but state no published data? Data will become available and can then be included in the future.

Thank you for this consultation opportunity.

Yours faithfully
Alan Smith (On behalf of Medical Affairs, Gilead Sciences)

Graham Foster from Barts Health sent the following message:

The recommendation that patients with mild HCV and HIV should undergo therapy only as part of a clinical trial or if there is evidence of progressive disease on fibroscan or other non-invasive test is based on a number of unproven assumptions.

It is assumed that the new, interferon free regimes will be equally effective in co-infected patients. Given that sofosbuvir (the lead agent) has reduced efficacy in cirrhosis, reduced response rates in men (not at all clear why) and very poor response rates in G3 this is a dangerous assumption. It is probable that response rates will be reduced in co-infection (and we have no data to tell us how reduced they will be) and co-infected patients may require therapy of longer duration. The costs and provision of this are unclear. If sofosbuvir response rates in G1 patients with HIV are reduced to to the level seen in G3 we will require a new series of phase 3 trials with extended duration/ multiple drug combinations before we have effective regimes and we may be some years away from this. At the very least patients and clinicians need to be aware that there is great uncertainty about the new regimes in co-infection and this uncertainty is not adequately expressed here.

It is assumed that non-invasive markers will reliably predict disease progression. I am not aware of any properly powered study assessing the sensitivity and specificity of these tests in this context. Given the confounding factors in fibroscan (fat deposition, inflammation etc are known to modify liver stiffness) it is unwise to base critical management decisions on these tests and, again, the guidelines need to reflect the uncertainty - the studies to-date are too small and the follow up too short to know the power of these assays in detecting disease progression over the medium term.

The underlying assumption is that the new drugs will be funded and will be funded for all patients - even those with mild disease. Given the constraints on the health care budget and the clear view expressed here - 'patients with mild disease do NOT need treatment' - I do not think we can guarantee that funding will be provided for expensive therapies in patients with early disease. This may be a particular problem in co-infection where, I suspect, more complex (aka expensive) regimes may be required. This recommendation may well come back to haunt BHIVA - if I was purchasing health care from a limited budget I would use this statement to justify withholding therapy from patients with HCV and mild disease.

The public health dimensions are not discussed adequately. Given the infectious nature of HCV, treating IDUs or active MSMs who are transmitting the virus seems a very sensible thing to do.

Whilst I share the sentiment behind the recommendation - patients with early HCV should think very carefully about their choices and not rush into therapy - this statement is too strong. It is not evidence based, relies on assumptions that are unproven and exposes all of our patients to funding constraints. I think that in the current climate a recommendation NOT to treat early HCV is most unwise and this statement should be modified.

Dr Gopinath Ranjith from Faculty of Liaison Psychiatry, RCPsych sent the following message:

Please consider adding the following recommendation under Section 8.6.1 between recommendations 86 and 87:

We recommend referral to liaison psychiatry services for patients with pre-existing mental health problems prior to initiation of therapy and for patients with treatment-emergent psychiatric problems during therapy to improve adherence with treatment.

This can be a GPP but references to support the recommendation (even if in the treatment of hepatitis C and not necessarily in HIV/hepatitis co-infection) include

Lotrich FE (2013) Psychiatric clearance for patients started on interferon-alpha-based therapies. *American Journal of Psychiatry*, 170: 592-7

Schaefer M et al (2012) Hepatitis C infection, antiviral treatment and mental health: A European expert consensus statement. *Journal of Hepatology*, 57: 1379-90.

Neri S et al (2010) A multidisciplinary therapeutic approach for reducing the risk of psychiatric side effects in patients with chronic hepatitis C treated with pegylated interferon α and ribavirin. *Journal of Clinical Gastroenterology*, 44: e210-7.

BASHH BBV SIG COMMENTS ON DRAFT BHIVA HEPATITIS GUIDELINES 2013

Collated by Laura Waters (BASHH BBV SIG Chair) 25th June 2013

(SENT BY FILE ATTACHMENT)

HAV vaccination: recommendation 26 to vaccinate all HIV+ against HAV differs from BHIVA immunisation guidelines (which recommend vaccinating those at risk of HAV or its complications only, ie not all HIV-positive per se) – will the immunisation guidelines be updated accordingly? Should the website include a note that where recommendations differ between guidelines the most recent guideline should be used? Does the guideline need to note that the advice differs from the older immunisation guidelines and therefore supersedes it? The new guidance would mean vaccinating far more individuals than we do currently.

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- Vaccination – note the shift away from rapid protocols which have become very popular in sexual health clinics this may need some additional highlighting although the rationale is laid out just a bit of a culture shift.

HBV screening:

- Ongoing screening for HBsAg even if vaccinated (4.4.1.33) – thjs is a bit easier from an order set point of view but is likely to have a very low yield in a vaccinated population. Is this really justified? Again labs might be a bit concerned at the mass of tests heading their way.

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Unexplained transaminitis:

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From Dola Awoyemi (and to be accompanied by edited file she sent)

Please note that for table 8.2 I have ;
- removed the off-label comment "75kg: 1000mg; ≥ 75kg: 1200mg [off-label]" as this dose banding refers to genotype 1 only.
- included genotype 4 for the Copegus dose of 800mg daily.
- removed all unlicensed comments i.e. asterix and footnote

For table 8.2 I have amended the increase in Cmin for BOC (to 4%) and Rilpivirine (to 51%)

BW

Dola Awoyemi

Farhad Cooper

Dear Dr Wilkins

Many thanks for your recent consultation regarding updating the current Hepatitis B guidelines. I have recently been working on a project with Dr Ann Sullivan, at Chelsea and Westminster, to better utilise the principles of contact tracing and prevention of new Hepatitis B infections in at risk groups, a practice that is well established in the GU clinic setting for other communicable diseases. I hoped I could share some of our experiences with you, and make some suggestions with explanations of our rationale, for your working group's consideration.

Current NICE Guidelines on contact tracing / partner notification / screening and vaccination

Current NICE guidelines on Hepatitis B ¹ say very little about the role of contact tracing/partner notification, screening, and immunisation of at risk groups. It is interesting that a practice which has been mastered by the Genitourinary Medicine specialty has not been rigorously advocated nor implemented for Hepatitis B, an infection which is commonly transmitted in the UK through sex and sexualised drug use amongst high risk groups, as well as being prevalent amongst other hard to reach and engage groups.

Suggestions for new BHIVA Guidelines

NICE public health guidance 43 (March 2013)²– makes some excellent suggestions regarding how to reduce the morbidity and mortality due to new infections, which we have integrated into the new “Hepatitis B-Link”³ service that we are to begin to operate shortly.

It aims to bring a one-stop integrated service for patients that takes place alongside their first / subsequent hepatitis clinic appointments, to maximise impact and minimise the risk of a loss to follow-up.

I would like to propose that BHIVA also advocates the same, in order to bring us into line with current NICE public health guidelines on the management of Hepatitis B.

These suggestions are as follows:

To provide when possible at the same time and place of the first appointment:

- 1) partner notification / contact tracing. This will include a discussion about common modes of transmission and advice regarding screening/vaccination for those from high prevalence regions.
- 2) the opportunity to give out printed literature in various languages / access to online resource in various languages / information regarding various ways in which partners can be contacted (PN slips / electronically / SMS etc).
- 3) should a patient attend with a companion, they will also be offered the chance to have a discussion with us about points (1) and (2). If they consent, they can have screening and vaccination performed there and then, and be informed about follow up with us.

As well as the following at subsequent appointments:

- 4) revisit the issue of PN / contact tracing, and also assess progress and collect data regarding how many contacts have been contacted by the patient / have been screened so far.

Evidence / References

Reference 1

NICE Hepatitis B (Chronic) full guideline (DRAFT January 2013) – pages 6, 11, 12, 13, 17, 21-25

Reference 2

NICE public health guidance 43 (march 2013) – pages 45, 60, 66

Reference 3

“Hep B Link”, as the project is called, is an “on demand” service, that creates a one-stop integrated service which makes use of our expertise in areas such as screening, contract tracing / partner notification and vaccination, and ensures seamless transition to care between the two services.

It is hoped that by providing an opportunistic service that takes advantage of time usually spent waiting for an appointment, patients will find this both useful and informative. It will also allow for health promotion to take place / additional information about sexual health services to be made available, and also assist the hepatitis clinic by occupying patients when they may otherwise be waiting.

Dr Farhad Cooper
SpR HIV and Genitourinary Medicine
Chelsea and Westminster Hospital

Jonty Manuja from Janssen sent the following message:

Janssen is committed to providing medicines that have a real impact on the lives of patients and reducing public health burdens, such as HIV. Janssen appreciates the opportunity to consult on the draft BHIVA co-infection guidelines and would like to commend the writing committee on the methodology employed.

Please see below for detailed comments by section:

8.5 Choice of ART

Section 8.5.1 Recommendations

This section states in the recommendations: We recommend if telaprevir is to be used, either RAL or standard-dose ritonavir-boosted atazanavir should be used: efavirenz may be used but the telaprevir dose needs to be increased to 1125mg tds.

Janssen believes rilpivirine deserves to be mentioned as an ‘alternative’ option in treatment naive patients with viral loads < 100, 000 cps/ml in the main recommendations rather than only the rationale section. We believe that the addition of rilpivirine to the recommendations would offer this patient group a greater choice, in addition to the benefits of a lack of clinically relevant drug-drug interaction requiring no dose adjustment of either drug or increased monitoring for adverse events.

Section 8.5.3 Rationale

In the rationale section etravirine is suggested as an alternative ARV to use with boceprevir (and telaprevir) and in table 8.2 ‘Interactions between ARVs and drugs used to treat HCV’, it is noted that when boceprevir and etravirine are used in combination no dose adjustment of boceprevir is required.

Pharmacokinetic data on this drug-drug combination showed a decrease in etravirine levels and boceprevir C_{min}, which has not been studied with a boosted PI. We believe wording to reflect the fact that the clinical significance of these reductions has not been directly assessed, and increased clinical and laboratory monitoring for HIV and HCV suppression is recommended, be added for clarity, as reflected in the boceprevir SmPC1.

8.5 Assessment and investigation

Section 8.6.3 Rationale

On page 71 the draft guidelines state: Several new agents are being studied both in the mono-infection and co-infection setting [74]. Early reports of two alternative protease inhibitors, faldaprevir and simeprevir in co-infection have shown high rates of RVR and eVR, comparable to mono-infection studies where these agents have been associated with higher rates of SVR than presently available PIs [75,76]. Studies of interferon-sparing approaches have commenced in the setting of HIV. Results of interferon-sparing approaches have, in the mono-infected population, shown very high rates of response with relatively short periods of treatment [77].

Janssen requests that the statement “Early reports of two alternative protease inhibitors, faldaprevir and simeprevir in co-infection have shown high rates of RVR and eVR, comparable to mono-infection studies where these agents have been associated with higher rates of SVR than presently available PIs [75,76]” be removed or changed to reflect the lack of increase in efficacy seen (described below).

The studies QUEST-1 (simeprevir; reference 75) and STARTVERSO1 (faldaprevir; reference 76) demonstrated SVR rates of 80% and 79-80% respectively in treatment naive patients. The ADVANCE phase 3 study of telaprevir demonstrated an SVR rate of 79% in treatment naive patients. Furthermore, although not head to head studies, the delta was highest in the ADVANCE study; 33% vs 30% for QUEST-1 and 27-28% for STARTVERSO-1.

Janssen would also request it is made clear that simeprevir and faldaprevir are given in combination with PEG-IFN and ribavirin.

On page 71 the draft guidelines state: Treatment with boceprevir and telaprevir have the disadvantages of requiring co-prescribing of PEG-IFN and ribavirin, difficult dosing schedules as both must be administered three times a day; difficult toxicity profiles (anaemia, neutropenia and dysgeusia with boceprevir; and anaemia, skin rash [including Stevens–Johnson syndrome] and anal discomfort with telaprevir); multiple drug interactions (including with components of ART); and cost.

Janssen believes that co-prescribing of PEG-IFN and ribavirin is not a disadvantage for telaprevir or boceprevir as the drugs in development, discussed earlier (simeprevir and faldaprevir), will also be used in combination with PEG-IFN and ribavirin.

Following a recent change to the SmPC, telaprevir is now licensed for 1,125mg bid dosing². Janssen requests that this be considered in the section above. We acknowledge there might be concerns with telaprevir-ARV drug-drug interactions when using bid dosing in coinfection but feel that not mentioning the bid dose may cause confusion to prescribers and patients.

Janssen would like to also request that “[including Stevens–Johnson syndrome]” be changed to “[including rare cases of Stevens–Johnson syndrome]”. In the Phase 2 and 3 clinical trial programme less than 0.1% of patients had SJS².

As telaprevir and boceprevir are both NICE approved drugs for the treatment of chronic G1 HCV (including in co-infection), Janssen believes that cost cannot be described as a disadvantage as they have been proven to be cost effective vs PEG-IFN and ribavirin alone.

On page 73 of the draft guidelines table 8.2 ‘Adverse event and pharmacokinetic profiles of hepatitis therapy’, Janssen suggests the following additions are made:

Boceprevir: Neutropenia is not mentioned as a side effect of boceprevir but within the boceprevir SmPC¹ it states the addition of boceprevir to peginterferon alfa–2b and ribavirin resulted in higher incidences of neutropenia and Grade 3-4 neutropenia compared with peginterferon alfa–2b and ribavirin alone.

Telaprevir: As described above, telaprevir is now licensed 1,125mg bid and Janssen feels the table should reflect this. We acknowledge there might be concerns with telaprevir-ARV drug-drug interactions when using bid dosing in coinfection but Janssen thinks that not mentioning the bid dose may cause confusion to prescribers and patients.

To note, telaprevir is also not licensed for use in decompensated liver disease.

Section 8.7 Antiviral treatment: genotype 1

8.7.1 Recommendations

This section states in the recommendations: We recommend where there is a current clinical need for treatment, or if the patient wishes to be treated, the standard of care should be with triple therapy consisting of pegylated interferon, ribavirin, and either telaprevir or boceprevir (1C).

Given the evidence below for the use of telaprevir and boceprevir based triple therapy in co-infected patients Janssen believes that this recommendation should be graded (1A).

- NICE TAG252 concludes that telaprevir plus peginterferon alfa and ribavirin was clinically more effective than peginterferon alfa and ribavirin alone in inducing a sustained virological response in previously untreated and previously treated patients, ICERs represent a cost-effective use of NHS resources and should be recommended as an option for the treatment of genotype 1 chronic hepatitis C in adults with compensated liver disease who are previously untreated or in whom previous treatment has failed. The Committee considered what impact excluding from trials patients co-infected with HIV and intravenous drug users had on the generalisability of the results to the UK population. It concluded that although these patients were not represented in the pivotal clinical trials, based on the current evidence available, there was no reason to make any different provision for these patients.
- NICE TAG 253 concludes that boceprevir plus peginterferon alfa and ribavirin was clinically more effective than peginterferon alfa and ribavirin alone in inducing a sustained virological response in treatment-naïve patients and previously treated patients, irrespective of baseline fibrosis level, ICERs demonstrate that boceprevir represents a cost-effective use of NHS resources for patients with genotype 1 chronic hepatitis C. The Committee considered the use of Boceprevir plus peginterferon alfa and ribavirin in patients with HCV infection who are co-infected with HIV. Although these patients were not represented in the pivotal clinical trials, based on the current evidence available, the Committee concluded that there was no reason to make any different provision for these patients.
- Study 1103 was a randomised, double-blind, placebo controlled trial of Telaprevir in HIV/HCV co-infection which demonstrated an increase in SVR and a similar side effect profile to telaprevir in the treatment of HCV mono-infection
- Boceprevir has also been studied in a randomised, double blinded, placebo controlled trial⁴ which demonstrated an increase in SVR and a similar side effect profile to boceprevir in the treatment of HCV mono-infection
- The ANRS cohorts of telaprevir⁵ and boceprevir⁶ treated HIV/HCV patients have both shown early efficacy at week 16 of treatment in HCV treatment experienced patients with more advanced liver disease
- A cohort report from the US⁷ has shown higher SVR rates in an HIV/HCV patient population than a HCV mono-infected. Similar adverse event profiles were reported between the two groups.

This section also states in the recommendations: We recommend for patients with genotype 1 infection and non-cirrhotic disease, treatment should be either within a clinical trial or deferred until newer therapies become available (GPP).

Janssen fully appreciates the importance of participation in clinical trials and agrees that patients should be offered the choice of participation in a clinical trial or treatment on the NHS.

Janssen believes that PI based HCV treatment should not be necessarily be deferred in patients who are non-cirrhotic. Given the considerations described below and NICE approval of telaprevir and boceprevir regardless of stage of liver disease, Janssen requests that this recommendation be reconsidered to include offering triple therapy to all patients irrespective of

stage of liver disease provided the patient wishes to be treated. Deferring patients for treatment until the newer agents have secured HTA approval would be for an unspecified period of time with an uncertain outcome and with clinical implications for patients in whom the disease is unpredictable and more rapid in its progression.

Efficacy of current and new therapies decreases in patients with cirrhosis

SVR rates for patients with compensated cirrhosis deteriorate with telaprevir² and boceprevir⁸ in the HCV mono-infection setting. Furthermore, data from the PIs in development also show lower SVR rates in patients with cirrhosis, for example in the QUEST-1 study of simeprevir + PEG/RBV in HCV mono-infection, SVR decreased from 83% in F0-2 patients to 78% in F3 patients to 58% in F4 patients.

Faster Clinical Progression in patients co-infected with HIV/HCV

As described in these guidelines, observational data demonstrate that individuals with HCV co-infection have faster rates of fibrosis progression and an increased risk of cirrhosis, ESLD, HCC and liver-related death than those with HCV mono-infection (reference 43). Although the recommendation of close monitoring of liver disease are welcomed, it is of concern that HCV related liver disease progression is not linear. A study in HCV mono-infection has shown inter-patient variability in rates of progression in similar follow up periods⁹.

Treating patients now reduces further transmission

Outbreaks of HCV within the HIV+ MSM community have been well documented, as noted on page 26 of these guidelines. By deferring treatment in non-cirrhotics until newer agents become available, more transmission is likely to occur in this population, resulting in increased number of patients needing treatment in the future.

Preventing Cirrhosis

Patients with cirrhosis of the liver are at increased risk of hepatocellular carcinoma (HCC) and surveillance should, as per the UK guidelines for the management of suspected HCC in adults¹⁰, be considered in all males and females with cirrhosis. If surveillance is offered, it should be using six monthly abdominal ultrasound assessments in combination with serum alpha-fetoprotein estimation. Preventing HCV related cirrhosis of the liver by treating patients with less advanced liver disease would reduce the need for six monthly HCC surveillance which would have economic and healthcare resourcing implications.

Treating HCV has shown to improve Quality of Life

Data from the 2009 US National Health and Wellness Survey showed patients with HCV were significantly less likely to be employed compared with controls ($p < 0.0001$)¹¹. The presence of HCV in the EU population has been shown to significantly impact several domains of HRQL ($p < 0.05$)¹². In the telaprevir ADVANCE trial, obtaining an SVR was significantly associated with an improvement health related quality of life at week 72¹³.

A recent study also showed HCV eradication had a beneficial effect on cerebral metabolism and selective aspects of neurocognitive function¹⁴.

The UK consensus guidelines do not differentiate when to start therapy based on cirrhosis

The UK consensus guidelines¹⁵ for the use of the protease inhibitors boceprevir and telaprevir in genotype 1 chronic hepatitis C infected patients were written with the aim to suggest current best practice for treating G1 HCV with telaprevir or boceprevir based triple therapy. These guidelines recommend that protease inhibitor based regimens should be considered for all genotype 1 chronic HCV-infected patients.

This section also states in the recommendations: We recommend non-cirrhotic patients who were previously null responders, partial responders or who experienced breakthrough should, wherever possible, wait for the availability of interferon-sparing regimens or interferon-based regimens including at least two new agents (GPP).

Janssen would again suggest that PI based treatment be offered to previously treated relapsers and partial responders, irrespective of stage of liver disease. In mono-infection, data from the REALIZE trial in treatment experienced patients showed that previous relapsers has an SVR rate of 84% and previous partial responders had an SVR rate of 61%². Furthermore, initial data from the ANRS cohort^{5,6} shows high rates of undetectable HCV RNA in coinfecting patients at week 16 who were previous relapsers or partial responders to PEG-IFN and ribavirin. Janssen agrees with deferring treatment at patients request in previous null responders.

On page 77 the draft guidelines state ‘Both telaprevir and boceprevir have drawbacks which include toxicities, drug–drug interactions with antiretrovirals and other commonly used agents, thrice-daily dosing, and both must be administered with PEG-IFN and RBV’

Janssen would like to request reference to twice daily dosing for telaprevir. We acknowledge there might be concerns with telaprevir-ARV drug-drug interactions in coinfection when using bid dosing but feel that not mentioning the bid dose may cause confusion to prescribers and patients.

On page 77 the draft guidelines state ‘Telaprevir is dosed three times daily in combination with PEG-IFN and RBV. There is preliminary data on administering telaprevir twice daily.’ This data on twice daily dosing is now within the label for Telaprevir².

¹Boceprevir SmPC

²Telaprevir SmPC

³Sulkowski MS, et al. Hepatology 2012;54(Suppl.1):219A

⁴Mallolas J, et al. J Hepatol 2012;56 (Suppl 2):S22

⁵Cotte L, et al. CROI 2013, Abstract 36

⁶Poizot-Martin I, et al. CROI 2013, Abstract 37

⁷Martel-Laferrriere et al. CROI 2013, Abstract 679

⁸Vierling et al., EASL 2013, Abstract 1430

9Boccatto S, et al. J Viral Hepat 2006;13:297–302

10UK guidelines for the management of suspected HCC in adults

(<http://www.mccn.nhs.uk/userfiles/documents/04a%20HCC%20guidelines%20accepted%20version%20march%2009.pdf>)

11DiBonaventura M, et al. J Med Econ 2011;14:253–61

12DiBonaventura M, et al. Eur J Gastroenterol & Hepatol 2012;24:869–77

13Younossi Z, et al. DDW 2012; Poster 1048

14Byrnes V, et al. J Hepatol 2012;56:549–56

15Ramachandran et al., Aliment Pharmacol Ther 2012; 35: 647–662

Robert James from BHIVA Hepatitis Society sent the following message:

I contacted a group of community activists in coinfection to comment on these guidelines. This is a synthesis of their responses. Others took the opportunity to respond individually or on behalf of their organisations.

Firstly it is great that these guidelines have come out. A number of features were specifically pleasing to people in the community, the expansion of coverage to include all the hepatitis viruses, some of the tables that express complex material well such as 8.2 on DDIs comparing Boceprevir and Telaprevir with ARVs, and, the mention of HCV prevention amongst MSM with HIV - even if only to highlight our current lack of proven interventions.

Below are the comments as that refer to specific recommendations.

Testing and prevention

Rec 14 While the IL28b test not being standard makes good sense as it is only relevant for a patient in making a decision to take treatment or not it is likely to remain a useful test for some years to come. Interferon is likely to remain an important part of treatment for the next few years with additional DAAs rather than exclusively DAAs. Genotype 2, and possibly 3 if longer duration of treatment is effective, are probably the only ones that are likely to have licensed interferon free combinations in the next couple of years meaning that interferon will remain a mainstay of treatment for a while yet. The IL28b will therefore remain a useful indicator of the value of taking treatment now or waiting where a person has the option. In cost terms interferon is likely to be cheaper than any of the upcoming DAAs and so, ignoring the bloody awful side-effects in most people, it may be a cheaper way of curing people.

Rec 19 The addition which would be most helpful for non-expert clinicians would be a clearer description of what the evidence is on the potential risk factors for HCV transmission. The known risky behaviours are listed but a bit more narrative explaining how strong the evidence is for each one would be helpful. There is one paragraph within 4.2.3 that describes sexual transmission and cites 11 studies but is more about correlations with risk factors such as concomitant STI infections, rather than the strength of evidence for specific practices being relevant to HCV transmission.

There is little about how a clinician should identify if a patient is at high risk of HCV transmission beyond the results of blood tests for ALT, other STIs, etc. Continuing injecting drug use is probably one such indicator although it is not clearly highlighted but it is unclear what a clinician should be looking for amongst MSM with HIV, is it any unprotected anal intercourse, or a specific frequency, or only in conjunction with fisting, or multiple partners in single venues,

etc. If a distinction for monitoring purposes is going to be made then how that is done is not particularly clear in the guidelines – it may be that the problem is that there is a lack of clarity about how to do this proactively which might be worth stating. Even if this decision to enhance PCR monitoring is usually going to be a reactive one to blood test results and therefore logically after risk events it can be of value.

Rec 21 The recommendation for non-invasive tests as “the investigation of choice” is welcome, especially by haemophiliacs with HIV/HCV coinfection. Having a range of indicators though can lead to the situation of different levels of fibrosis suggested in the same patient by the different tests. Although the guidelines do state that Transient Elastography [TE] “outperform blood panels” it is somewhat buried in the text and reversing the last 2 paragraphs of 4.3.3 may make it clearer. The text would then read more logically starting with biopsy as a gold standard of accuracy but is an invasive procedure, highlight TE as the next best and finally blood panel algorithms.

Vaccinations for HBV

Rec 29 This is quite comprehensive but for those patients who do not respond after a second batch of three doses, or whose titres remain <10 IU/L when should the vaccine be re-tried in them? Never, when their CD4 count rises above a certain figure, (maybe 500 cells/ μ L as despite weak evidence it is the figure for the accelerated dosing schedule) or after a period of time such as 3 or 5 years?

Hep C treatment

Rec 38 The issue of DDIs when using DAAs on ART is going to be problematic for some years to come and the intervention of a specialist pharmacist would be very helpful here. Why not recommend all patients are assessed by specialist pharmacists before starting their treatment for HCV, if this is not already routine practice in clinics?

Rec 72 All supported more frequent monitoring of HCV-PCR in people with repeated high risk exposures but there was uncertainty about how these patients would be identified. A number may well self-identify but others will probably be more reticent to disclose high risk practices and it may be incumbent on the medic to ask. It is believed by people in the community that MSM who engage in high risk sexual practices have quite good awareness of HCV and that some practices, notably fisting, are linked to its transmission but it is unknown how many are comfortable discussing this with their HIV doctor. It was highlighted that the criminalisation of STIs may also inhibit frank discussions between doctor and patient here (and HCV amongst MSM with HIV would be legally considered to be an STI). Identification will become important as more and more stable patients on ART move to annual monitoring of HIV rather than 4-6 monthly. At the moment this may only be something being done at the request of long standing patients but it is likely to become more common in the future as it is cheaper and takes up less of the patients time.

Rec 93 This recommendation is unclear. 48 weeks are recommended for genotype 1 but 24 may be ok? Would it not be better to specifically state that 24 weeks could be considered for those treatment-naïve patients without cirrhosis who have an RVR.

Helen Donovan from Royal College of Nursing sent the following message:

Comments collated from various members with particular interest:

In general the guidelines are clear and fit in with best practice and the RCN feel applicable.

- The guidelines are evidence based and provide clear guidance for the treatment of HIV and Hepatitis
- We would urge for the comments of people living with HIV and/or hepatitis should be considered to ensure that there is full involvement in the final guidelines and also in HIV care
- In addition HIV support organisations and services should be highlighted to ensure that patients have access to relevant peer support help if required.

Yusef Azad from NAT (National AIDS Trust) sent the following message:

BHIVA GUIDELINES FOR THE TREATMENT AND MANAGEMENT OF CO-INFECTION WITH HIV-1 AND HEPATITIS VIRUSES 2013

NAT submission to consultation

Introduction:

NAT (National AIDS Trust) is the UK's leading charity dedicated to transforming society's response to HIV. We provide fresh thinking, expertise and practical resources. We champion the rights of people living with HIV and campaign for change.

NAT welcomes the chance to comment on the draft BHIVA Guidelines on HIV/hepatitis C co-infection. In particular, the rise in co-infection amongst MSM in the UK has been a matter of serious concern and prompted NAT to publish a report 'Hepatitis C and HIV Co-infection' in January 2012. In our response to the draft Guidelines we will focus solely on the issue of the prevention and diagnosis of Hepatitis C amongst MSM living with HIV since this is the area where we have done previous detailed work.

NAT's report called for HIV/Hep C co-infection to become a strategic priority within gay men's health promotion. We re-stated the importance of the annual Hepatitis C screen for all people living with HIV, in light of the significant percentage of people with HIV in the BHIVA 2009/10 audit who were not being offered an annual hepatitis C screen.

In relation to BHIVA, the report identified a lack of clarity in the Guidelines as to which patients should be offered 'more frequent than annual', i.e at least six monthly, hepatitis C testing on the basis of sexual risk. We said there was a need for a consensus to be secured as to 'key risk factors for the sexual transmission of hepatitis C'.

Hepatitis C testing for patients living with HIV:

It is good to see the recommendation of a hepatitis C test at diagnosis and then at least annually restated clearly.

It is also good to see more frequent testing recommended of between three and six months for those with high risk sexual behaviours - though this recommendation is somewhat obscured and could usefully be stated simply and clearly in the screening, prevention and immunisation section at the outset of the document. We discuss below how 'high-risk sexual behaviours' are defined in the draft Guidelines and the need for greater clarity.

It is a bit unclear whether section 4 is meant to cover screening just at diagnosis (the title of section 4.2) or look more broadly at ongoing needs for screening and prevention – the content sometimes seems to possibly refer just to diagnosis and sometimes to ongoing interventions, including behavioural. Even if some recommendations are repeated elsewhere in the Guidelines, we propose section 4 on Screening, prevention and immunisation cover both the period immediately after diagnosis and also the period of ongoing care, that recommendations for each period, or both, are clearly identified, and that all relevant recommendations on screening, prevention and immunisation are included in this section.

When the reader turns to section 8.3 for recommendations on more frequent hepatitis C testing, the focus appears to be less on the relevant risk factors for more frequent testing, or how frequent such testing should be, and more on the type of test to be used – the two issues are conflated in the recommendations. It can result in recommendations which are quite complicated and opaque to read, for example the final one at section 8.3.1.

The Guidelines do not state explicitly how high-risk sexual behaviours and the need for hepatitis C testing might come to the attention of the HIV/GU clinic. The BHIVA Guidelines for the routine investigation and monitoring of adults with HIV do recommend six monthly comprehensive sexual history taking, and this could usefully be referred to in the co-infection Guidelines text.

The one reference to monitoring is at section 8.3.3 where it says that ‘it is important to monitor previously infected individuals frequently’ given significant rates of hepatitis C re-infection.

Given that three monthly hepatitis C testing is suggested as one option there could usefully be some content on the frequency with which patients with HIV are monitored in relation to risk of hepatitis C transmission, and any instances where more frequent monitoring even than the six monthly norm is considered appropriate.

High-risk sexual behaviours:

Recent high-risk exposure is described in section 8, dealing with ongoing hepatitis C testing of people with HIV, as ‘e.g unprotected sex between men, sharing drug injection paraphernalia’.

In the Rationale to section 4 there is a different and more specific list of sexual risk factors including multiple sexual partners, infection with syphilis, gonorrhoea and LGV, insertive anal intercourse and use of douches or enemas. In the earlier counseling section ‘mucosally traumatic sexual practices’ such as ‘fisting and use of sex toys’ are mentioned, along with ‘group sex activities, recreational and intravenous drug use, and condomless anal intercourse’.

We understand that more research is needed on the precise mechanisms and most significant routes of hepatitis C infection through sexual exposure. But the references to different sexual risk behaviours in different sections of the same document simply reinforce confusion and inconsistency, and in NAT’s view militate against real progress in focused, targeted and effective counseling and testing for hepatitis C.

To give one example of a possible impact, in the important section 8 where three to six month repeat testing is recommended for those at high risk, the two behaviours cited are ‘unprotected sex’ and ‘sharing drug injection paraphernalia’. There is an ‘e.g’ before them but it is nevertheless unhelpful not to mention here, for example, fisting, use and sharing of sex toys, group sex sessions and use of crystal meth, mephedrone or GHB/GBL. Is there value in being more explicit in recommendations and auditable outcomes on the heightened risk to MSM (the one reference around behaviour in recommendations seems to be to 'unprotected sex between men')?

NAT recommends that a consistent description of what is meant as high-risk behaviours for hepatitis C transmission risk is clearly set out and repeated in relevant contexts throughout the Guidelines.

It may be useful even within a description of high-risk behaviours to identify some of them as being particularly associated with hepatitis C transmission. For example, recreational drug use may well be a high-risk behaviour but it now appears that there is especially heightened risk from the current and increasing use of crystal meth, mephedrone and GHB/GBL. Unprotected sex between men is also a risk factor but perhaps especially so where both men are living with HIV. This may assist clinical decision-making as to whether to propose three- or six-monthly monitoring and testing, for example.

In the bullet points on 'Counselling on behaviour modification' included within section 4 it seems strange that the list of 'potential risk factors' for hepatitis C transmission is included in the third bullet point on advice to patients diagnosed with hepatitis C, but there are no risk factors listed in the second bullet on advice to all patients with HIV. The recommendation above on a consistent list of risk factors repeated whenever appropriate would address this. We commend BHIVA for including this section on prevention within the Guidelines.

Conclusion

NAT believes the current revision of the co-infection Guidelines is an immensely important opportunity to improve the prevention and diagnosis of hepatitis C amongst HIV positive MSM. Engagement with their HIV clinic on a regular and ongoing basis may well be for most HIV positive MSM at risk of hepatitis C the one clinical opportunity there is to provide prevention interventions and diagnose hepatitis C promptly. HIV/GU clinics need to work to prioritise reductions in hepatitis C transmission, and reductions in late hepatitis C diagnosis, amongst HIV positive MSM.

When we published our report on ‘Hepatitis C and HIV Co-infection’ we wrote formally to BHIVA drawing our recommendations and conclusions to BHIVA’s attention, and asking that a session on hepatitis C prevention and testing be regularly included in the BHIVA conferences on the Management of HIV/Hepatitis C Co-Infection. We regret this has not yet happened and that again this year there is no session dedicated to this issue. NAT recommends that sessions on hepatitis C prevention and testing, especially for HIV positive MSM, be regularly included in conferences on hepatitis C/HIV co-infection organised by BHIVA and other relevant clinical

bodies.

NAT July 2013

Eilish McCann from Merck Sharp & Dohme sent the following message:

MSD welcome the opportunity to consult on the draft BHIVA guidelines for the treatment and management of co-infection with HIV-1 and hepatitis viruses.

MSD would like to note that although the need to provide “good practice points” where an insufficient evidence base exists is recognised, we kindly request that BHIVA consider the implications of making non-evidence based recommendations for the use of licensed medicines in a way which is inconsistent with the marketing authorisation, or recommending delay in treatment in favour of investigational compounds which have not yet, and may not, gain a licence or reimbursement in HIV/HCV coinfecting patients.

Please see our associated email for detailed comments tabulated by the section of the guideline they refer to. (SEE ASSOCIATED EILISH MCCANN DOCUMENT)

Keith King from Homerton Dept of Sexual Health sent the following message:

In the section on counselling and behaviour modification it says "19. We recommend risk reduction advice should be given to patients diagnosed with HCV and should incorporate information about potential risk factors for HCV transmission, including mucosally traumatic sexual practices (i.e. fisting, use of sex toys), group sex activities, recreational and intravenous drug use, and condomless anal intercourse (GPP)." I would suggest including potential household exposure including sharing of toothbrushes, razors, etc.

In section 8.6 Assessment and investigation - is there a need to put something in about routine mental health screening prior to commencement on Peg-Riba+PI therapy or does the statement "85. We recommend all patients with HCV/HIV infection should be assessed for suitability for treatment of hepatitis C (GPP)." capture it? Mental Health assessment is also described in the rationale, so perhaps specific mention in the recommendation is not necessary.

**British HIV Association Hepatitis Consultation
RCGP Response
– Dr Matthew Hoghton, Medical Director of CIRC &
Danny Morris, RCGP Substance Misuse and Associated Health**

The RCGP welcomes the updating of BHIVA Guidelines for the treatment of management of co-infection with HIV-1 and hepatitis viruses. These are comprehensive and well researched guidelines and the RCGP recognises the considerable amount of work and expertise that has gone into their production. There are a few minor points

Dr Matthew Hoghton:

1. The title of the guidelines suggests comprehensive age coverage though the scope in 1.1 advises "best clinical practice in the treatment and management of adults with HIV and viral hepatitis co-infection " with no apparent signposting to guidelines to children or adolescents.

2. Special situations that the guidelines could consider addressing

2.1 Recommendations for Co-Infected pregnant Women other than table 8.2 on Page 73

2.2 Co-infected parents and protection of children

2.3 Co-infected people who are in prison

2.4 Co-infected people in other institutions

2.5 Co-infected people who are sex offenders

2.6 Co-infected health workers

2.6 Co-infected people who are sex industry workers

2.7 Co-infected people who lack capacity

Danny Morris:

2: Should be clear that recommendations to support 'standard practice'. 'We recommend' or 'we suggest' are too wooly.

4.2.1 – no. 19: “recreational and intravenous drug use...” - Should be recreational, including intravenous drug use. The rise in injecting among the gay party scene is recreational rather than dependent. Dr Owen Bowden-Jones at the London Drug Club Clinic would be able to inform in more detail on this as 'slamming' or injecting crystal meth and/or mephedrone parties are notably on the rise with reports of sharing injecting equipment a norm.

3.2: adults/patients should be actively involved in all aspects of treatment

3.4: Active engagement of people with HIV and/or hepatitis is central in maximising treatment adherence

8.7.1, Fifth bullet point - This is a potential contradiction of the third bullet point - is there a argument to offer treatment for G1 rather than defer as significant proportion will still achieve favourable outcomes?

General comment: There are a number of varying treatment regimens - these might be better visually represented with diagrammatic pathways.

We hope these comments are helpful and are grateful for the opportunity to contribute.