Comments on ACD for Hepatitis C 2006

Consultee and commentator responses

Consultee	Section	Comment	Action
Clinical expert	1.8 and 1.9	I agree that the current dataset does not permit a firm conclusion to be drawn regarding re-treatment, therapy in children and therapy for those who have undergone liver transplantation. However the tone of these recommendations (treatment is not recommended) is a little robust and might dissuade clinicians from attempting therapy when there are extenuating circumstances. For example my own practice is to offer therapy to teenage children who are concerned about transmission and I would consider therapy for a patient with mild hepatitis C who had received a second liver transplant if HCV recurrence had led to loss of the first graft (there is some anecdotal data to suggest that patients who develop aggressive HCV recurrence in a transplanted liver may do so again if they are retransplanted for recurrent HCV). I appreciate that these are unusual circumstances but the statement that treatment should NOT be given may make it difficult to obtain support for therapy in these unusual circumstances. I would therefore prefer a slightly more guarded statement such as:-	1.8 in ACD (1.5 in FAD) no change regarding second or subsequent courses of treatment
		‘There is insufficient data to assess the value of therapy for people with mild hepatitis C who are younger than 18 years or those who have had a liver transplant. Therapy would not normally be considered appropriate for such patients.” This will dissuade clinicians from treating such patients but will not act as an absolute barrier in unusual circumstances.	Suggestion accepted.

Consultee	Section	Comment	Action
	Section 2.2	'Page 5 para 2.2 is ambiguous. In the setting of acute infection most people are asymptomatic but 20% do develop symptoms and occasionally jaundice. Many chronically infected patients are polysymptomatic and suffer from vague non-specific symptoms. I suggest that the first two sentences be re-written to read:- People acutely infected with hepatitis C are often asymptomatic, but about 20% will develop overt hepatitis. Many chronically infected patients will experience non-specific symptoms including malaise, weakness and anorexia.'	Changed as suggested
Association of Nurses for Substance Abuse	4.3.11	Section 4.3.11 relates to continued IVDU / alcohol consumption. This section remains unclear for practitioners and leads to differences in practice around the country. This is clearly an area for more research and audit (section 5). In particular, many vulnerable patient groups at which testing is being targeted, fail to undertake testing, as they often perceive that they will not get treated if found to have CHC. Further research should be encouraged particularly as early virological responses for Genotypes 2/3 may enable shortened treatment courses, which would be invaluable for vulnerable groups such as those with drug misuse issues, rough sleepers, prisoners, sex workers etc. More qualitative research should be encouraged to look at the impact of Multi-disciplinary team working / clinical managed networks that can support these groups of people and aim to reduce rates of further infections (affecting public health issues).	Outside the scope of this appraisal. Suggest as a research question

Consultee	Section	Comment	Action
British Society for Gastro-enterology		In general, this document does provide a suitable basis for the preparation of guidance to the NHS. However, I believe that the Appraisal Committee's preliminary recommendation 1.9 is contentious. I am not clear whether a Paediatric Hepatologist was involved in preparing the Appraisal Consultation Document. I think that recommendation 1.9 would be better phrased "We are not making recommendations for people with mild chronic hepatitis C who are younger than 18 years, or those who have had a liver transplant". I do not believe it is possible to recommend that these groups of patients should not have combination therapy on current available evidence. As is pointed out in the report, individuals with mild chronic hepatitis C infection have a better response rate than those with more advanced disease. Likewise, hepatitis C infection of any severity has a stigma attached for infected children, perhaps preventing them leading a full and active lifestyle, so it would seem reasonable that some children with mild chronic hepatitis C infection should be considered for treatment. Likewise, although sustained virological response rates following treatment of patients with chronic hepatitis C infection after liver transplantation are poor, undoubtedly 15 to 20 per cent of patients will have a sustained virological response. herefore I do not think it is reasonable on current evidence to say that combination therapy is not recommended for those who have had a liver transplant.	As for clinical expert's point Stigma is now mentioned in 4.3.11. Committee cannot recommend for children, as it cannot recommend off-licence.
Foundation for Liver Research		Agree with ACD	No action required
Haemophilia Society		A delay in the full review date to from November 2006 is entirely sensible. We are interested in refinements to the interferon-treatment regimes, particularly if it is possible to reduce the duration of therapy without impacting on predicting success rates, but defer to clinical experts for guidance on whether November 2008 is a suitable point in time for the next full review. Should any new treatments for chronic hepatitis C be licensed, we would also urge NICE to begin a new appraisal process for these in a timely fashion.	Noted

Consultee	Section	Comment	Action
Hep C Trust		We have, however, a few minor points: Para 1.8. I suspect the word 'sustained' is not intended. A reduction in viral load at 12 weeks is an 'early' response. Paras 1.8 and 1.9. The wording of both paragraphs suggests that retreatment in the specified circumstances and treatment of those transplanted or under 18 are prohibited. We would be happier if they stated that there is insufficient evidence to make recommendations. Para 2.3. The words 'which affects the ability of the virus of the immune system to mount an effective response' should be omitted. They are unnecessary and suggest more is understood about the inter-relation between the virus genotype and the immune system than is currently the case. Para 7.3.6 (and presumably point 6 on page 37). This is a restatement of para 1.8 so 'sustained' should be replaced by 'early'. We believe that November 2008 is an excellent time for a review as it should coincide with the availability of trial data for at least 2 new drugs being fast-tracked for approval by the FDA in the US.	 Changed as suggested Changed – see response to clinical expert above Omitted as suggested Changed as suggested for 7.3.6. Point 6 in appendix refers to "sustained" and not "early"
MRC Clinical Trials Unit		Agrees with ACD	No action required
RCGP		Agrees with ACD	
RCN		No further comments	

Consultee	Section	Comment	Action
RCPathol		In the review of the scoring systems used to assess chronic hepatitis C liver biopsies on page 25 it is stated that Metavir scores necroinflammatory grade on a scale of 0 to 3. This is not accurate. The Metavir paper scores activity (grade) as piecemeal necrosis from 0 to 3 and lobular necrosis from 0 to 2. In this respect it is analogous to the other systems in separating the components of piecemeal necrosis and parenchymal necroinflammatory activity. Fibrosis (stage)) is correctly quoted as being scored from 0 to 4.	Refers to assessment report
		In the first bullet point at the bottom of page 26 it is true that biopsy may not give a representative picture of liver pathology. However liver biopsy in chronic hepatitis C always identifies the minimum level of disease activity and stage that is present.	Refers to assessment report
		If the NICE recommendation remains that mild chronic hepatitis C should be treated with pegylated interferon and ribavirin then it follows that a liver biopsy to differentiate mild from moderate chronic liver disease and thus select patients suitable for treatment is no longer required. The points made in the above paragraphs will not influence that recommendation. Subsequently the indications for liver biopsy in any particular patient with chronic hepatitis C will then be determined by other clinical criteria.	Noted
NHSQIS I	General	There are 2 typographical errors in the evidence in section 3.3, the dose of peg Interferon Alfa 2b should 1.5mcg/kg and not 180 mcg as stated. The error is repeated twice in that section.	Changed as suggested
NHSQIS II	3.3	A. Section 3.3. There is a mistake in the dose of peginterferon alfa-2b which should read 1.5 micrograms/kg rather than 180 micrograms.	Changed as suggested
	3.2 and 3.3	B. Sections 3.2 and 3.3. The statements that patients with genotypes 1, 4, 5 and 6 may be eligible for shorter duration (at least 24 weeks) of combination therapy if the viral load is low are premature. No definition of low viral load is given and individual manufacturers assays are variable and not standardised.	

Consultee	Section	Comment	Action
NHSQIS II (continued)		The latest manufacturers summary of product characteristics refer to this area as follows: Viraferonpeg - For patients who exhibit virological response at week 12, treatment should be continued for another nine month period (i.e., a total of 48 weeks). In the subset of patients with genotype 1 infection and low viral load (<600,000 IU/ml) who become HCV-RNA negative at treatment week 4 and remain HCV-RNA negative at week 24, the treatment could either be stopped after this 24 week treatment course or pursued for an additional 24 weeks (i.e. overall 48 weeks treatment duration). However, an overall 24 weeks treatment duration may be associated with a higher risk of relapse than a 48 weeks treatment duration. Pegasys – patients infected with genotype 1 regardless of viral load should receive 48 weeks of therapy. C. Sections 1.4 and 7.3.4. There is increasing literature on the possibility of treating patients with genotypes 2 and 3 infection with shorter courses of therapy (12, 14 and 16 weeks) provided there is an EVR at 4 weeks (Hepatology 2004;40:1260-5; Gastroenterology 2005;129:522-7; NEJM 2005;352:2609-17). Perhaps the committee should consider this area as patients with mild disease are more likely to respond readily.	4.3.7 now contains a discussion of this point. Changed as suggested Not licensed for this indication.

Consultee	Section	Comment	Action
NHSQIS III	General	I am not sure if the papers looking at early viral response to therapy have been looked at. There is evidence that some patients with genotype 1 virus with a low load may only require 24 weeks of treatment if there are signs that they are responding to treatment.	As for NHSQIS II.
		Patients with genotype 2 and 3 who are responding to treatment with suppression of their viral load may only require between 12 and 16 weeks of treatment	As for NHSQIS II
		If the above were to be considered then the cost effectiveness may be more evident	As for NHSQIS II
		I agree with the recommendations to treat patients (with all genotypes) with mild disease but the duration of therapy may be shortened in some instances (see above). This should be referred to in the final document.	
NHSQIS IV	General	This is, as usual, a comprehensive and thoughtful review of the use of antiviral therapy for mild and moderate hepatitis C infection, and the conclusions reached are well supported by the evidence. I know of no other significant evidence not considered, and would expect the conclusions to be as valid in Scotland as in England.	Noted

Consultee	Section	Comment	Action
Roche		**a) Licensed indications of pegylated interferons** The specifics of the licensed indications of the two pegylated interferons have not wholly been taken into account when formulating the draft guidance. An important distinguishing factor exists between the two respective licensed indications. The licensed indication for pegylated interferon alfa-2a permits the treatment of patients with normal and elevated ALT levels. However, the licensed indication for pegylated interferon alfa-2b only permits the treatment of those patients with elevated ALT. A proportion of normal ALT patients will have mild disease; therefore to recommend pegylated interferon alfa-2b as a treatment option for all mild patients, is endorsing a use which is outside of license. The guidance should therefore make explicit that pegylated interferon alfa-2b should only be recommended for use in mild patients with elevated ALT only.	This is taken into account by use of the words "within their licensed indications" in section 1 of the guidance. The point is noted and agreed, but the phrase "within their licensed indications" covers the point already.
Roche (continued)	1.3	**b) Recommendation of watchful waiting strategy** Paragraph 1.3 of the guidance states that: *"the decision as to whether a person with mild CHC should be treated immediately rather than waiting until the disease has reached a moderate stage (watchful waiting) should be made by the person after fully informed consultation with the responsible clinician".* This appears to provide an implicit recommendation within the guidance to "watch and wait" without a clear definition of the circumstances under which this is considered the optimal treatment choice. The recommendation appears to contradict the available evidence base which demonstrates that the decision to treat early with pegylated interferon compared to the decision to "watch and wait" is cost effective (section 4.6.2 of the ACD). Consequently the statement perhaps gives the impression that the option to "watch and wait" is being recommended within the guidance, in addition to the option to treat with pegylated interferon.	The discussion on this point is covered already in 4.3.14.

Consultee	Section	Comment	Action
		c) Pegylated interferon as an "option" for treatment of mild CHC It is not clear to us why pegylated interferon is only being recommended as an option when section 4.2.7.3 of the ACD states that compared to conventional interferon pegylated interferon is cost effective. In addition, compared to the option to watch and wait prior to treatment within the moderate/severe setting, pegylated interferon is also cost effective. Consequently Roche suggests that pegylated interferon is recommended for the treatment of mild CHC and not stated as an "option" within the final guidance.	The words 'as an option' have been omitted from 1.1 and 1.2. To avoid confusion of comparison of PEG versus IFN with mild versus moderate.
Roche (continued)		**a) Progression rates from mild to moderate/severe CHC** Section 2.2 appears to provide slightly conflicting messages over the rate of progression of this disease describing the rate as "slow yet variable". Also the sentence that states: "30% of those infected develop cirrhosis within 20-30 years" should be clarified to state that this is from the time of infection and not diagnosis. In general, the guidance perhaps appears to cast an unnecessary level of uncertainty over CHC progression and its potential impact upon the cost effectiveness of treating mild CHC patients. Sensitivity analysis performed on the cost effectiveness results within the Assessment Report (P.126-127) illustrated that the rate of progression from mild to moderate disease was not a sensitive parameter upon the final ICER. Roche has not identified any evidence base that demonstrates: • evidence of lower rates of progression from mild to moderate disease compared to those presented in the assessment report; • threshold level of progression rates that would lead to the treatment of mild patients with pegylated interferon's not being cost effective.	No change "from time of infection" added.

Consultee	Section	Comment	Action
		Consequently, sections 4.2.1, 4.3.9 and 4.3.10 should be amended because presently the evidence of slower progression rates and the potential impact of this on the cost effectiveness of treatment is extremely weak and only serves to undermine the relatively high degree of certainty around the cost effectiveness of these treatments	4.2.1 is a conditional statement and does not need to change. It has been moved to the considerations section. 4.3.9 and 4.3.10 also are statements of our lack of knowledge. In the absence of any evidence to refute the wording in these sections, no change has been made.
		b) Off-license assessment of pegylated interferon alfa-2b dose In section 4.1.8 the description of "low dose pegylated interferon alfa-2b" plus ribavirin that achieved an SVR of 51% is an "off-licence" dosing schedule and is inappropriate to evaluate the efficacy of pegylated interferon alfa-2b.	Noted
Roche (continued)	4.2.7.2	**c) Cost per QALYs listed** It is unclear within section 4.2.7.2 whether the cost per QALYs listed are reflective of the early stopping rules recommended in section 1.4 to 1.7 of the guidance. We would suggest the definitive cost per QALYs listed within the guidance should be consistent and representative of these.	Clause added to this effect.
		a) Budget Impact of Pegylated interferon alfa 2a Our original submission provided an estimate of the likely NHS budget impact of implementing pegylated interferon alfa-2a for the treatment of mild CHC compared to current standard practice. Assuming current practice within the NHS is to watch and wait amongst mild CHC patients, the drug acquisition costs of implementing pegylated interferon will be additive and consequently will require additional budget allocations.	Noted. Refer to Implementation and costing group

<table>
<tr><th>Consultee</th><th>Section</th><th>Comment</th><th>Action</th></tr>
<tr><td>Roche (continued)</td><td></td><td>
b) Summary of Roche budget impact of Pegylated interferon alfa 2a for the treatment of mild CHC
We estimated a constant 19% diagnosis rate of hepatitis C patients and of all patients diagnosed, 25% were assumed to have mild hepatitis C. Of the total budget impact we presented, a phased implementation of any guidance, growing from 20% diffusion in year 1 to 100% diffusion by year 5.
These results are summarised in the table below:
Assuming a Constant 19% Diagnosis Rate and 25% of patients diagnosed having mild HepC
<table>
<tr><th></th><th>Year 1</th><th>Year 2</th><th>Year 3</th><th>Year 4</th><th>Year 5</th></tr>
<tr><td>Number of Hepatitis C patients</td><td>3,802</td><td>3,802</td><td>3,802</td><td>3,802</td><td>3,802</td></tr>
<tr><td>Number of Genotype 1 patients</td><td>2,586</td><td>2,586</td><td>2,586</td><td>2,586</td><td>2,586</td></tr>
<tr><td>Peginterferon alfa-2a with ribavirin</td><td>£23,037,857</td><td>£23,037,857</td><td>£23,037,857</td><td>£23,037,857</td><td>£23,037,857</td></tr>
<tr><td>PCR Testing</td><td>£168,069</td><td>£168,069</td><td>£168,069</td><td>£168,069</td><td>£168,069</td></tr>
<tr><td>Less cost of liver biopsy</td><td>£1,935,461</td><td>£1,935,461</td><td>£1,935,461</td><td>£1,935,461</td><td>£1,935,461</td></tr>
<tr><td>Annual Budget Impact</td><td>£21,270,466</td><td>£21,270,466</td><td>£21,270,466</td><td>£21,270,466</td><td>£21,270,466</td></tr>
<tr><td>Annual Budget Impact, assuming a staggered NICE Implementation</td><td>£4,254,093</td><td>£8,508,186</td><td>£12,762,280</td><td>£17,016,373</td><td>£21,270,466</td></tr>
</table>
</td><td>Noted. Refer to Implementation and costing group</td></tr>
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Consultee	Section	Comment	Action
Roche (continued)		The above results illustrate that if only 19% of patients are actually diagnosed and 25% of these have mild CHC, assuming all of these patients are then treated, a total of approximately £21.3m will be required to implement the guidance. Close joint working will be required between NHS commissioners and providers; and between departments within NHS Trusts in order to ensure that appropriate funds and services are made available in a timely manner to enable proper implementation of the guidance.	
		c) Payment by Results (PBR) tariff Currently the treatment of hepatitis is excluded from the range of PbR tariffs. However, once fully implemented it will be critical that an appropriate PbR tariff is set to enable successful implementation of this guidance. The tariff must sufficiently reimburse NHS Trusts for using pegylated interferon in order to avoid any "perverse incentives" to utilise alternative less expensive forms of treatment for mild CHC.	Outside scope of the appraisal.
		d) NHS Capacity Considerations Again when fully implemented, the guidance will potentially have a large impact upon the number of eligible patients requiring treatment. Consequently, the necessary service delivery resources must also be planned for and made available. For example, relative to cancer and cardiovascular disease, hepatitis is often not viewed as a high public health priority amongst NHS Trusts and consequently special attention may be required to ensure that this guidance is properly implemented in a timely manner.	Noted. Refer to Implementation and costing group.

Consultee	Section	Comment	Action
Schering-Plough		***Use of peginterferon alfa-2b in genotype-1 low viral load patients*** We would like to draw attention to the fact that the ACD does not refer to the use of peginterferon alfa-2b (ViraferonPeg) as being considered for use in genotype 1 patients, with low viral load, in mild and moderate to severe hepatitis C, which is within our licensed indication. As noted in the S-P submission to NICE (May 2005), section 2.3.3.1, '*genotype 1 patients should be treated for the full 48-week period assuming they are viral negative at 12 weeks and 24 weeks. However, for a subgroup of these patients, genotype 1, low viral load (LVL), treatment may be shortened to 24 weeks only if genotype 1 LVL patients are viral negative as early as week 4'*. Applying this stopping rule would reduce the average cost per course of therapy to £6,553, for genotype 1 patients with LVL, for 24 weeks of treatment.	The guidance no longer specifies duration of treatment for each circumstance. Prescribers should refer to the relevant SPC.

Consultee	Section	Comment	Action
Schering-Plough (continued)		Additionally, as clearly stated in the summary of product characteristics (SPC), genotype 1 patients with low viral load may only require 24 weeks of treatment: As per section 4.2 of the SPC: *'Genotype 1: For patients who exhibit virological response at week 12, treatment should be continued for another nine month period (i.e., a total of 48 weeks).* *In the subset of patients with genotype 1 infection and low viral load (< 600,000 IU/ml) who become HCV-RNA negative at treatment week 4 and remain HCV-RNA negative at week 24, the treatment could either be stopped after this 24 week treatment course or pursued for an additional 24 weeks (i.e. overall 48 weeks treatment duration). However, overall 24 weeks treatment duration may be associated with a higher risk of relapse than 48 weeks treatment duration.'* In contrast to the above, in section 3.2 of the ACD, it is stated that *'for genotypes 1, 4, 5 and 6, the regimen is peginterferon alfa-2a 180 micrograms once per week (low viral load) or for 48 weeks (high viral load) plus ribavirin 1000mg per day (< 75kg body weight) or 1200 mg day (>75mg) for the same length of time as peginterferon alfa'*. However, as stated in the summary of product characteristics for peginterferon alfa-2a (Pegasys), section 4.2, *'the duration of combination therapy with ribavirin for chronic hepatitis C depends on viral genotype. Patients infected with HCV genotype 1 regardless of viral load should receive 48 weeks of therapy'*. There is, therefore, no distinction made between low and high viral load in the license for peginterferon alfa-2a and all genotype 1 patients receive 48 weeks of treatment.	Amended in FAD

Consultee	Section	Comment	Action
Schering-Plough		We would like to draw attention to the following errors that have been detected in the ACD that are in contrast to the results of the HTA report. • The dose of peginterferon alfa-2b (ViraferonPeg), used in combination with ribavirin (Rebetol), in genotype 2/3 patients. • The dose of peginterferon alfa-2b (ViraferonPeg) used in combination with ribavirin (Rebetol), in genotype 1, 4, 5 and 6 patients. • The cost of treatment of peginterferon alfa-2b (ViraferonPeg) and ribavirin (Rebetol) for genotype 1 patients and genotype 2/3 patients. • The cost of treatment of peginterferon alfa-2b (ViraferonPeg) monotherapy for genotype 2/3 patients and all other genotypes. The cost of treating genotype 2/3 patients and genotype 1 patients with combination therapy peginterferon alfa-2b (ViraferonPeg) and ribavirin (Rebetol) is les than that stated in the ACD. Additionally, the cost of monotherapy for treating genotype 1 patients with peginterferon alfa-2b (ViraferonPeg) is less than the cost of treating the same patients with peginterferon alfa-2a (Pegasys).	Amended in FAD

Consultee	Section	Comment	Action
Schering-Plough		***Dosing of Treatment*** Section 3.3 of the ACD refers to peginterferon alfa-2b (ViraferonPeg) and ribavirin (Rebetol) and states that *'for genotypes 2 and 3 the licensed regimen is peginterferon alfa-2b 180 micrograms once per week plus ribavirin 800 mg per day (< 65 kg body weight) or 1000 mg per day (65–85 kg) or 1200 mg per day (> 85 kg) for 24 weeks'.* This is not the licensed regimen for peginterferon alfa-2b (ViraferonPeg) used in combination with ribavirin (Rebetol) for genotype 2/3 patients. As stated in the SPC, section 4.2, the licensed dose of peginterferon alfa-2b is 1.5 micrograms/kg/week in combination with ribavirin capsules, for 24 weeks, for these patients. In the same section, it is stated that '*for genotypes 1, 4, 5 and 6, the licensed regimen is peginterferon alfa-2b 180 micrograms once per week for at least 24 weeks (low viral load) or for 48 weeks (high viral load) plus ribavirin 800 mg per day (< 65 kg body weight) or 1000 mg per day (65–85 kg) or 1200 mg per day (> 85 kg) for the same length of time as peginterferon alpha'.* Again, this is not the licensed regimen for peginterferon alfa-2b (ViraferonPeg) used in combination with ribavirin (Rebetol). As stated in the SPC, section 4.2, the licensed dose of peginterferon alfa-2b is 1.5 micrograms/kg/week in combination with ribavirin capsules. The duration of treatment may vary from 24 to 48 weeks for genotype 1 and genotype 4 patients.	Amended in FAD

Consultee	Section	Comment	Action
Schering-Plough	Section	***Cost of Treatment*** According to the ACD, the cost of treating genotype 1 patients with peginteferon alfa-2b (ViraferonPeg) and ribavirin (Rebetol) is £13,468, for 48 weeks of treatment and the cost of treating genotype 2/3 is £6,734, for 24 weeks of treatment. In the HTA report, page 111, section 5.4.5.5, it is clearly stated that the cost of treating genotype 1 patients with combination therapy peginterferon alfa-2b (ViraferonPeg) and ribavirin (Rebetol) is £13,106, for 48 weeks treatment, while the cost of treating genotype 2/3 patients is £6,553 for 24 weeks. When referring to the cost of treatment with peginterferon monotherapy, section 3.3 states that 'for genotypes 2 and 3 the cost of peginterferon monotherapy is £3,169 (for 6 months), and for other genotypes £6,339 (for 12 months) for other genotypes'. It should be clearly stated that the latter cost refers to the cost of monotherapy treatment of all genotypes with peginterferon alfa-2a (Pegasys) and ribavirin (Copegus). In the HTA report, page 111, section 5.4.5.5, it has been calculated that the cost of peginterferon alfa-2b (ViraferonPeg) monotherapy for treatment of genotype 1 patients is £5,261, for 48 weeks of treatment and £2,631, for 24 weeks of treatment.	Amended in FAD
DoH		No comments	
Wales HSB		HCW has approved individual patient requests from clinicans for the use of this drug combination for Welsh resident patients. All approvals are on an individual approval basis".	Noted

Responses from non-consultees/commentators

Role	Section	Comment
NHS professional	1	What about Genotypes 2s; would it not be cost effective to test their viral load at WK 4 if HCV RNA not detected duration of therapy 12 weeks. (Delgard 2004). Like wise for genotype 3 low viral load.
	2.10	2:10 This belief that biopsy should not be performed on geno 2 and 3 may have a negative impact on the NHS in the future. Not always does the LFTS and PLTS and INR markers inform us that a pt IS cirrhotic. And with the demand on clinic space within the NHS genotypes 2 and 3 pts not being biopsy; commence therapy; subsequently clear their virus and are discharge from the NHS back to the GP care. A small percentage may be cirrhotic and even though their clear virus may decompensate if not monitored by their GPs. I believe that if we are to exclude biopsing these individuals we should either be introducing the fibroscan into the NHS or keeping at least yearly reviews on these pts
	5	Afro -Americans/ Afro- Carribeans are known not to respond as well as Causcains however there is not study investigating why. Or whether with this population the outcome for embarking therapy should be improving histological of liver, lowering vrial load and normalising LFTS than terminating their therapy at week 12 because EVR is not been achieved
NHS professional	1.5	.Why does everyone lump genotypes 4,5 and 6 like geno 1. Genotype 4 mainly cccurs in Egypt, what is the evidence for 12 weeks EVR predicting 48 week response? The data on Geno 4 is weak and there are suggestions periods of treatment longer than 48 weeks are needed - more data is needed here. I am not aware of any studies in Geno 4 and mild disease
	3.3	Can you not even get the dose of viraferonpeg right!! It is a weight based regime, it is pegasys which is one dose for all!