Consensus Meeting on Therapy for Chronic Hepatitis C
London March 3 2015

Background

The treatment options for patients with chronic hepatitis C are expanding rapidly. To guide clinicians and commissioners the national societies (BASL, BIA, BSG, BVHG) representing clinicians with an interest in this area convened a meeting to provide evidence based treatment and management recommendations.

Methods

A nominated individual outlined the background data (both published and outcome data from the English early access program) and presented proposals for therapy. These were discussed by the 80 attendees and a consensus was reached. This document outlines the consensus recommendations.

Treatment recommendations:

Genotype 1 - Patients with no evidence of cirrhosis/severe fibrosis

For patients who are treatment naïve preferred treatment is with all oral direct acting antiviral regimens. The following options are all acceptable on efficacy and safety criteria:-

Sofosbuvir/Ledipasvir+/- ribavirin*	8 weeks
Ombitasvir/Paritaprevir (r)/Dasabuvir +/- ribavirin*	12 weeks
Sofosbuvir/Simeprevir	12 weeks
Sofosbuvir/Daclatasvir	12 weeks

If oral DAA regimens are not funded for this patient group by the NHS, patients have the option of waiting for oral therapy, self-funding or starting treatment with an interferon-based regimen.

Interferon based regimes include:-

Sofosbuvir/PEG-interferon/Ribavirin	12 weeks
Simeprevir/PEG-interferon/Ribavirin	
G1b or G1a without Q80K variant	12 weeks plus 12 or 36 weeks PEG/RBV

For patients with G1a who are Q80K variant negative simeprevir based regimes are not recommended.

Genotype 1 Patients with compensated cirrhosis/severe fibrosis/major extra-hepatic manifestations

Preferred treatment is with all oral direct acting antiviral regimens. The following options are all acceptable on efficacy and safety criteria:

Ombitasvir/Paritaprevir (r)/Dasabuvir +/- ribavirin*	12 weeks (Child Pugh A only)
Sofosbuvir/Ledipasvir+/- ribavirin*	12 weeks
Sofosbuvir/Simeprevir +/- ribavirin	12 weeks
Sofosbuvir/Daclatasvir +/- ribavirin	12 weeks

For all other patients who have failed to achieve SVR with PEG-interferon/Ribavirin treatment is as above (i.e. as per G1 compensated cirrhosis). However for patients with genotype 1a virus, and previous null response to PEG-interferon/Ribavirin, treatment should be 24 weeks of Ombitasvir/Paritaprevir (r)/Dasabuvir/Ribavirin.

For patients who have failed to achieve an SVR with PEG-interferon/Ribavirin and a protease inhibitor treatment should avoid a protease containing regime and preferred treatment options are sofosbuvir plus ledipasvir OR sofosbuvir plus daclatasvir.

Genotype 1 - Patients with decompensated cirrhosis

Treatment is recommended with oral Sofosbuvir/Ledipasvir +/- Ribavirin for a total of 12 weeks
**Strong consideration should be given to adding ribavirin, though individual patient decisions are to be made by MDT*

Genotype 2 - Patients with no evidence of cirrhosis/severe fibrosis

Treatment naive
PEG-interferon/Ribavirin 24 /52 (12/52 in low viral load/Rapid viral response)
Treatment experienced (previous PEG-interferon/Ribavirin), or IFN intolerant Sofosbuvir/ribavirin or those with extrahepatic manifestations 12/52

Genotype 2 - Patients with compensated cirrhosis/severe fibrosis/major extra-hepatic manifestations

Treatment naive:	Sofosbuvir/Ribavirin 12/52
Treatment experienced:	Sofosbuvir/Ribavirin 12/52 (cirrhotics 16/52)

Genotype 2 - Patients with decompensated cirrhosis

Treatment is recommended with either
Sofosbuvir/Ledipasvir +/- Ribavirin for a total of 12 weeks

Sofosbuvir/Daclatasvir +/- Ribavirin for a total of 12 weeks

Genotype 3 - Patients with no evidence of cirrhosis/severe fibrosis

For patients who are treatment naïve preferred therapy is:-

PEG-interferon/Ribavirin for 16-24 weeks

For those intolerant of interferon – Sofosbuvir plus daclatasvir +/- ribavirin for 12 weeks is recommended

For patients who are treatment experience preferred therapy is:-

PEG-interferon/Ribavirin /Sofosbuvir for 12 weeks

For those intolerant of interferon – sofosbuvir plus daclatasvir +/- ribavirin for 12 weeks is recommended.

Genotype 3 - Patients with compensated cirrhosis/severe fibrosis/major extra-hepatic manifestations

Preferred treatment is:-
PEG-interferon/Ribavirin /Sofosbuvir for 12 weeks

For those intolerant of IFN the following treatment options are all acceptable:-

Sofoabuvir/daclatasvir/ribavirin for 12 weeks
Sofosbuvir/ledipasvir/ribavirin for 12 weeks
Sofosbuvir/ribavirin for 24 weeks

Genotype 3 - Patients with decompensated cirrhosis

Treatment is recommended with either
Sofosbuvir/Ledipasvir +/- Ribavirin for a total of 12 weeks

Sofosbuvir/Daclatasvir +/- Ribavirin for a total of 12 weeks

Genotype 4 - Patients with no evidence of cirrhosis/severe fibrosis Non-cirrhotic G4 patients

Preferred treatment is for 12/52 therapy with all oral direct acting antiviral regimens. The following options are all acceptable on efficacy and safety criteria: choice to be determined by NICE approval, availability of funding from NHS England, and local MDT choice:

PEG-interferon/Ribavirin /Sofosbuvirfor 12/52
Ombitasvir/paritaprevir/ritonavir/ribavirin for 12/52
Sofosbuvir/Ledipasvir/ribavirin for 12/52

Genotype 4 - Patients with compensated cirrhosis/severe fibrosis/major extra-hepatic manifestations

Sofosbuvir/Ledipasvir/ribavirin for 12/52

Should none of the options above be available, patients wishing to be treated should be offered Simperevir/PEG-interferon/ribavirin with 24-48 weeks therapy (response guided therapy)

Genotype 4 - Patients with decompensated cirrhosis

Treatment is recommended with either
Sofosbuvir/Ledipasvir +/- Ribavirin for a total of 12 weeks
Sofosbuvir/Daclatasvir +/- Ribavirin for a total of 12 weeks

Liver transplant patients

Evidence of fibrosis post-transplant should mandate therapy as current data suggest that earlier treatment delivers comparable outcomes to non- transplant, non-cirrhotic populations. Therapy options can impact on immunosuppression thus monitoring and therapy should be delivered by, or in close collaboration with a transplant centre. Peg-interferon can precipitate graft rejection and its use can no longer be justified for the majority of transplant patients.
Options:

G1 sofosbuvir/ daclastavir +/- ribavirin – 12 weeks
sofosbuvir/ ledipasvir +/- ribavirin – 12 weeks
ombitasvir/paritaprevir (r)/dasabuvir/ribavirin 24 weeks
sofosbuvir/ simeprevir +/- ribavirin- 12 weeks

G3 sofosbuvir/ daclastavir +/- ribavirin – 12 weeks
sofosbuvir/ ledipasvir +/- ribavirin – 12 weeks

G4 sofosbuvir/ ledipasvir +/- ribavirin – 12 weeks
ombitasvir/paritaprevir/ritonavir/ribavirin- 12 weeks

Cirrhotic post –transplant are a small population and treatment should be individualized – ie no recommendations can be made due to a paucity of data

Other general recommendation:

- It is strongly recommended that all patients starting DAA therapy have a baseline plasma sample archived in the event of treatment failure. All patients with DAA failure should have a sample tested for relevant resistance on the first sample following failure
- In general, recommendations for HIV co-infected patients are the same as for mono-infection except where noted. Potential for drug-drug interactions should guide the choice of therapy. A useful website is http://hep-druginteractions.org/
- It is recommended that consideration is given to embedding strategically important research questions into the specialist commissioning process

Diagnosis of cirrhosis

The following working definition of 'cirrhosis/advanced fibrosis' was agreed for the sole purpose of including all/most patients likely to have cirrhosis due to hepatitis C* into the treatment algorithms proposed. Any one of the measures listed will suffice:

- Liver biopsy with stage 5/6 fibrosis
- Imaging evidence of cirrhosis (either US, CT or MR scan)
- APRI >2 and AST:ALT>1 on at least two occasions
- Evidence of established portal hypertension (varices or ascites) excluding non-cirrhotic or other causes
- Fibroscan elastography score >11.5 (or equivalent ARFI)

*where the patient has other risk factors for cirrhosis it will be for clinical judgement to consider the relative contribution from HCV and potential impact of treatment