

BHIVA guidelines for the management of hepatitis viruses in adults infected with HIV 2013

Update September 2014: Consensus statement on the guidelines for treating hepatitis C in patients with HIV

Further update due January 2015

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Consensus statement

Since the BHIVA guidelines for the management of hepatitis viruses in adults infected with HIV were published in January 2014, new data have been presented confirming the benefits of individual direct-acting antivirals (DAAs) with pegylated interferon (PEG) and ribavirin (RBV) and in combination in interferon-sparing regimens for the treatment of chronic hepatitis C (HCV). Several of these have now received European approval and other drugs are likely to be approved later in 2014 or in 2015. This update to the guidelines reflects the current situation and is intended to assist those involved in the management of chronic HCV/HIV co-infection, including patients, in making decisions on treatment. Updates to this guideline will be provided as and when new data become available.

General recommendations

1. The writing group recognise that availability of drugs and national or local directives may restrict the choice of options.
2. All patients with HCV/HIV co-infection should be seen in a specialist joint clinic by experienced physicians with a knowledge of HIV and HCV.
3. Patients with Child–Pugh B and C should be cared for in a transplant networked centre.
4. All patients should be considered for therapy irrespective of their fibrosis stage.
5. No patient should receive PEG if ineligible.
6. Only patients who have relapsed from pegylated interferon/ribavirin (PEG/RBV) therapy should be considered for retreatment with a PEG-containing regimen.
7. Patients with cirrhosis on therapy should be carefully monitored for decompensation irrespective of whether they are receiving PEG.
8. DAAs should form the backbone of all treatment options irrespective of genotype (GT), fibrosis stage or past treatment status.
9. All patients receiving DAA-based therapy or with GT5 or GT6 should be referred to, or be part of a formalised clinical network, with a specialist centre.
10. All patients should be considered for, and have access to, clinical trials of DAA-based regimens.
11. The options for treatment of acute HCV should be discussed with all patients and should cover the benefits of immediate versus deferred therapy.

Table 1. Updated recommendations for first- and second-line treatment of HCV in patients with HIV.

First-line options for treatment			Length of treatment (weeks)		References
			Naïve/relapse	Experienced	
GT1	SOF	PEG/RBV ¹	12	NR	[1–3]
		RBV	24	24	[4–6]
		DAC	12	24 ²	[7]
		SMP	12	24 ²	[8]
GT2	SOF	RBV	12	12	[1,5,6,9,10]
GT3	SOF	PEG/RBV ¹	12	NR	[11]
		RBV	24	24	[5,6,9,10]
GT4	SOF	PEG/RBV ¹	12	NR	[1]
Second-line options for treatment			Naïve/relapse	Experienced	References
GT1	SMP	PEG/RBV ^{1,3,4}	24–48	NR	[12–14]
GT3	SOF	DAC	24	24	[7]
GT4	SMP	PEG/RBV ^{1,4}	24–48	NR	[15]
	DAC	PEG/RBV ^{1,4}	24–48	NR	[16]
	SOF	RBV	24	24	[5,6,17]

Notes to Table

PEG: pegylated interferon; GT: genotype; RBV: ribavirin; SOF: sofosbuvir; DAC: daclatasvir; SMP: simeprevir; NR: not recommended.

1. Naïve/relapse and PEG/RBV eligible only.*
2. Consider 24 weeks with cirrhosis and/or prior null response to PEG/RBV +/- NS3/4 protease inhibitor.
3. Only GT1b or GT1a Q80K polymorphism negative.
4. Response-guided therapy (RGT).

*Patients who are ineligible for interferon and ribavirin therapy include those with:

- a. Current or prior psychiatric illness, poorly controlled epilepsy;
- b. Autoimmune hepatitis or other autoimmune disorders;
- c. Major uncontrolled depressive illness;
- d. Impaired bone marrow function;
- e. A history of pre-existing cardiac disease including arrhythmias;
- f. Advanced cardiac, renal or other systemic disease;
- g. Decompensated hepatic disease;
- h. Hypersensitivity to pegylated interferon or ribavirin;
- i. Significant intolerance to interferon with discontinuation because of an adverse event.

References

1. Lawitz E, Mangia A, Wyles D *et al.* Sofosbuvir for previously untreated chronic hepatitis C infection. *N Engl J Med* 2013; **368**: 1878–1887.
2. Kowdley KV, Lawitz E, Crespo I *et al.* Sofosbuvir with pegylated interferon alfa-2a and ribavirin for treatment-naïve patients with hepatitis C genotype-1 infection (ATOMIC): an open-label, randomised, multicentre phase 2 trial. *Lancet* 2013; **381**: 2100–2107.
3. Rodriguez-Torres M, Rodriguez-Orengo J, Gaggar A *et al.* Sofosbuvir and peginterferon alfa-2a/ribavirin for treatment-naïve genotype 1–4 HCV-infected patients who are coinfecting with HIV. *IDWeek*. October 2013, San Francisco, CA, USA. Abstract 714.
4. Lalezari LP, Nelson DR, Hyland RH *et al.* Once daily sofosbuvir plus ribavirin for 12 and 24 weeks in treatment-naïve patients with HCV infection: the QUANTUM study. *48th Annual Meeting of the European Association for the Study of the Liver*. April 2013, Amsterdam, the Netherlands. Abstract 845.
5. Sulkowski MS, Naggie S, Lalezari J *et al.* Sofosbuvir and ribavirin for hepatitis C in patients with HIV coinfection. *JAMA* 2014; **312**: 353–361.
6. Molina JM, Orkin C, Iser DM *et al.* All-oral therapy with sofosbuvir plus ribavirin for the treatment of HCV genotypes 1, 2, 3 and 4 infection in patients co-infected with HIV (PHOTON-2). *20th International AIDS Conference*. July 2014, Melbourne, Australia. Abstract MOAB0105LB.
7. Sulkowski MS, Gardiner DF, Rodriguez-Torres M *et al.* Daclatasvir plus sofosbuvir for previously treated or untreated chronic HCV infection. *N Engl J Med* 2014; **370**: 211–221.
8. Lawitz E, Sulkowski MS, Ghalib R *et al.* Simeprevir plus sofosbuvir, with or without ribavirin, to treat chronic infection with hepatitis C virus genotype 1 in non-responders to pegylated interferon and ribavirin and treatment-naïve patients: the COSMOS randomised study. *Lancet* 2014; **384**: 403–413.
9. Jacobson IM, Gordon SC, Kowdley KV *et al.* Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. *N Engl J Med* 2013; **368**: 1867–1877.
10. Zeuzem S, Dusheiko GM, Salupere R *et al.* Sofosbuvir and ribavirin in HCV genotypes 2 and 3. *N Engl J Med* 2014; **370**: 1993–2001.
11. Lawitz E, Poordad F, Brainard DM, *et al.* Sofosbuvir in combination with peg-IFN and ribavirin for 12 weeks provides high SVR rates in HCV-infected genotype 2 or 3 treatment experienced patients with and without compensated cirrhosis: results from the LONESTAR-2 study. *64th Annual Meeting of the American Association for the Study of Liver Diseases*. November 2013, Washington DC, USA. Abstract LB4.
12. Jacobson IM, Dore GJ, Foster GR *et al.* Simeprevir with pegylated interferon alfa 2a plus ribavirin in treatment-naïve patients with chronic hepatitis C virus genotype 1 infection (QUEST-1): a phase 3, randomised, double-blind, placebo-controlled trial. *Lancet* 2014; **384**: 403–413.
13. Manns M, Marcellin P, Poordad F *et al.* Simeprevir with pegylated interferon alfa 2a or 2b plus ribavirin in treatment-naïve patients with chronic hepatitis C virus genotype 1 infection (QUEST-2): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet* 2014; **384**: 414–426.
14. Dieterich D, Rockstroh J, Orkin C *et al.* Simeprevir with pegylated interferon/ribavirin in patients co-infected with chronic hepatitis C and HIV-1: week-24 interim analysis of the TMC435-C212 study. *20th Conference on Retroviruses and Opportunistic Infections*. March 2013, Atlanta, Georgia, USA. Abstract 154LB.
15. Moreno C, Hézode C, Marcellin P *et al.* Once-daily simeprevir (TMC435) with peginterferon/ribavirin in treatment-naïve or treatment-experienced chronic HCV genotype 4-infected patients: final results of a phase III trial. *J Hepatol* 2014; **60** (Suppl): S535.
16. Hézode C, Hirschfield GM, Ghesquiere Q *et al.* Daclatasvir plus peginterferon alfa and ribavirin for treatment-naïve chronic hepatitis C genotype 1 or 4 infection: a randomised study. *Gut* 2014; [Epub 30th July].
17. Ruane PJ, Ain D, Riad J *et al.* Sofosbuvir plus ribavirin in the treatment of chronic HCV genotype 4 infection in patients of Egyptian ancestry. *64th Annual Meeting of the American Association for the Study of Liver Diseases*. November 2013, Washington DC, USA. Abstract 1090.