Peer Review File

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Reviewer A

The authors provide readers with a well-organized commentary on the recently revised treatment guidelines for simplified and strengthened testing, prevention, and treatment for the global eradication of hepatitis C.

Authors:
Thank you for the generous comments.

Reviewer B

Appreciate the review on this important topic.

Can the authors refine the goals of the commentary?
Is the intent to emphasize HCV elimination in the US and or North America with the release of updated AASLD IDSA guidance and reiterate the AASLD IDSA Guidance simplified regimens? Or is the article intended to also discuss HCV elimination as a worldwide effort, that is is it intended to be read by a broader worldwide audience?
If that is the intent, then need to mention SOF/DAC for low and middle-income countries (with the use of generics) though in general simplified regimen guidelines have not yet been published for these regimens. Can the authors amend the introduction to make the intent clear?

Authors:
Thank you for the comment. Although the manuscript is intended to focus on the IDSA guideline focusing on HCV elimination in the US, we recognize the importance of mentioning the HCV elimination effort in low- and middle-income countries. We changed the manuscript and included the content as advised

The authors should include a sentence or short discussion on harm reduction measures given the strong link between hepatitis C and opioid use disorder

Authors
Thank you for the suggestions. We incorporated the harm reduction measures into the manuscript.

Page 5 regarding the comment that “It is important to mention that Sofosbuvir/velpatasvir plus weight-based ribavirin

90 are recommended for HCV genotype 3 with baseline NS5a (HCV nonstructural protein
91 5A) Y93 RAS (resistance-associated substitution) or decompensated HCV cirrhosis".
This should be revised to emphasize this is for those with compensated cirrhosis or decompensated cirrhosis. Those without cirrhosis and GT3 do not need RAS testing if receiving SOF/VEL.

Authors

Thank you. We modified our text as advised to reflect that Sofosbuvir/velpatasvir/ribavirin is indicated for the treatment of compensated cirrhotic patients infected with HCV genotype 3 and exhibiting either baseline NS5a (HCV nonstructural protein 5A) Y93 RAS (resistance-associated substitution) or decompensated HCV cirrhotic patients, irrespective of their HCV genotype or the presence of RAS.

Also, in the spirit of HCV elimination, for GT 3, how difficult will it be to send out an RAS analysis? Why not treat with SOF/VEL (or G/P) without RAS testing (which will be challenging to obtain in many elimination programs) and if no SVR is achieved then retreat with a salvage regimen?

Authors

Thank you. We modified our text as advised to mention that RAS is not readily available in many non-developed countries. Therefore, in pursuit of the global HCV elimination goal, We recommend treating the patients with SOF/VEL or G/P without the necessity of RAS testing, reserving the use of a salvage regimen for cases where SVR is not attained.

The authors should cite the importance of innovative reimbursement models (such as the subscription model being deployed by states such as Louisiana) as novel approaches to achieve HCV elimination in the US. The authors could also cite the HCV care model used to reduce the HCV burden in Egypt (N Engl J Med 2020; 382:1166-1174 if the article intends to discuss worldwide HCV elimination)

Authors

Thank you. We modified the manuscript as advised.

In the simplified treatment algorithm, the authors should discuss the need to determine the presence of cirrhosis and or advanced fibrosis and suggest methods as to how to determine this. While they conclude that it is not settled on whom to screen for HCC with advanced fibrosis, it is not controversial to screen those with cirrhosis due to HCV post-SVR for HCC and this should be emphasized.

Authors

Thank you. We modified the manuscript as advised.

The authors mention the missed doses algorithm in the AASLD/IDSA guidance. Can this be

added as a figure? It is a common question, particularly for those who are just becoming familiar with treatment for HCV infection, and a figure that can be referred to readily would be useful.

Authors

Thank you for the comments. We added a figure (Figure 2).

Reviewer C

The authors comment on a commitment to hepatitis C virus (HCV) eradication, including screening, prevention, and treatment. However, there are some concerns regarding this editorial commentary.

Major comments:

1. On pages 4-5, lines78-83, the authors describe the adaption and exclusion criteria for direct-acting antivirals. However, Glecaprevir/Pibrentasvir should be able to be administered to patients having HCV with end-stage renal disease.

Authors

Thank you for the comments. We removed the end-stage renal disease from the text as advised.

2. On page 6, lines 119-121, the authors stated the follow-up for non-cirrhotic patients who achieved a sustained virologic response (SVR). Do non-cirrhotic patients who achieved an SVR (other than those with an increased risk of reinfection or hepatocellular carcinoma) not need follow-up?

Authors

Thank you for the comments. We revised the paragraph to make it clear that non-cirrhotic patients with SVR do not require ongoing follow-up. However, cirrhotic patients with SVR would need ongoing follow-up for HCC screening.

Minor comment:

The American Association for the Study of Liver Disease and Infectious Disease Society of America should be abbreviated accordingly.

Authors

Thank you for the comments. We abbreviated both AASLD and IDSA accordingly.