DOI: 10.1111/apt.14083

WILEY AP&T Alimentary Pharmacology & Therapeutics

Letter: the efficacy of interferon-free regimens in HCV-related Child C cirrhosis needs careful interpretation

SIRS,

We read with great interest the systematic review project by Guarini et al., recently published in your journal.[1] Authors evaluated the efficacy of direct-acting anti-virals (DAAs) among hepatitis C virus (HCV) infected patients with Child C cirrhosis and reported a weighted mean sustained virological response (SVR 12) rate of 74.9% (95% CI: 65.6-82.4%). Limited data are available about using DAAs in HCV-related Child C cirrhosis and such valuable reviews may help for providing comprehensive evidence of using DAAs in this population. Here, we would like to highlight some points regarding this project.

First, Guarino et al. demonstrated that the most effective HCV treatment regimens in child C cirrhosis were sofosbuvir/ledipasvir, sofosbuvir/daclatasvir and sofosbuvir/simeprevir respectively. However, some issues should be more carefully addressed regarding the lower rate of SVR related to the sofosbuvir/daclatasvir regimen compared with sofosbuvir/ledipasvir. Authors pooled data from different studies regardless of their HCV genotypes. This point is important as sofosbuvir/daclatasvir is a recommended treatment option for HCV genotype 3, as the most difficult-to-treat HCV genotype in the era of DAAs.[2,3] In addition, as Guarino and coworkers showed, overall data related to sofosbuvir/daclatasvir are less than sofosbuvir/ledipasvir and according to the table 2 of Guarino et al.'s project, most studies evaluating sofosbuvir/ledipasvir have used ribavirin and/or treatment length of 24-week. Considering all of these conditions, it seems that efficacy of sofosbuvir/daclatasvir has been underestimated in this project.

Second, authors showed that neither administration of ribavirin nor lengthening treatment duration had a significant effect on the SVR rate. Importantly, it is in contrast with the suggestions of HCV treatment guidelines for using ribavirin or lengthening treatment duration among HCV-infected patients with decompensated cirrhosis.[2,4] Furthermore, although all interferon-free regimens are led to high rates of SVR, various DAAs have clearly different results.[5] In particular, available data have shown that combination therapy with sofosbuvir/simeprevir can lead to a lower rate of SVR in comparison with sofosbuvir/ledipasvir or sofosbuvir/daclatasvir.[4] Therefore, evaluating the effect of the treatment duration, ribavirin administration or interaction between them on the final SVR rates should be separated according to the regimen type. Otherwise, the results can be misleading.

Third, Guarino et al. recommended that protease inhibitors should be urgently evaluated in Child C cirrhosis. However, protease inhibitors should not be used in Child B cirrhosis and they are also contraindicated in Child C cirrhosis.[4]

Last, we believe that an appropriate meta-analysis for HCV treatment in the era of DAAs is the one that can adjust its final results regarding all factors affecting SVR rate like HCV genotype, administration of ribavirin, treatment length, cirrhosis status, comorbidities and etc.

In conclusion, we appreciate Guarino et al. for their nice project but emphasise that when there is insufficient data together with a considerable clinical heterogeneity, it would be better to do just a systematic reviewing of existing data instead of doing a meta-analysis.

ACKNOWLEDGEMENTS

Declaration of personal interests: None.

FUNDING INFORMATION

None.

LINKED CONTENT

This article is linked to Guarino et al and Andriulli et al papers. To view these articles visit https://doi.org/10.1111/apt.14017 and https://doi.org/10.1111/apt.14099.

M. S. Rezaee-Zavareh[1,2,3]
S. M. Alavian[2,3]
[1]*Student Research Committee, Baqiyatallah University of Medical Sciences, Tehran, Iran*
[2]*Baqiyatallah Research Center for Gastroenterology and Liver Diseases (BRCGL), Baqiyatallah University of Medical Sciences, Tehran, Iran*
[3]*Middle East Liver Diseases (MELD) Center, Tehran, Iran*
Email: Alavian@thc.ir

REFERENCES

1. Guarino M, Morisco F, Valvano MR, Ippolito AM. Systematic review: interferon-free regimens for patients with HCV-related Child C cirrhosis. *Aliment Pharmacol Ther* 2017;45:1193–1200.
2. Alavian SM, Hajarizadeh B, Bagheri Lankarani K, et al. Recommendations for the clinical management of hepatitis C in Iran: a consensus-based national guideline. *Hepat Mon*. 2016;16:e40959.
3. Alavian SM, Rezaee-Zavareh MS. Daclatasvir-based treatment regimens for hepatitis C virus infection: a systematic review and meta-analysis. *Hepat Mon*. 2016;16:e41077.
4. EASL. Recommendations on Treatment of Hepatitis C 2016. *J Hepatol*. 2017;66:153-194.
5. Hesamizadeh K, Sharafi H, Rezaee-Zavareh MS, Behnava B, Alavian SM. Next steps toward eradication of hepatitis C in the era of direct acting antivirals. *Hepat Mon*. 2016;16:e37089.