ANNALS of Hepatology

LIVER NEWS ELSEWHERE

September-October, Vol. 13 No. 5, 2014: 574-575

The good, the bad and the ugly of the new treatments for hepatitis C virus

Karen V. Silva-Vidal, Nahum Méndez-Sánchez

Liver Research Unit, Medica Sur Clinic & Foundation. Mexico City, Mexico.

Article commented:

Hagan LM, Sulkowski MS, Schinazi RF. Cost analysis of sofosbuvir/ribavirin versus sofosbuvir/simeprevir for genotype 1 hepatitis C virus in interferon-ineligible/intolerant individuals. *Hepatology* 2014; 60: 37-45.

Comment:

Approximately 185 million people worldwide have chronic hepatitis C virus (HCV) infection, and more than 350,000 people die of HCV-related liver diseases each year. Until 2011, the standard of care for patients with HCV genotype1 (GT1) was pegylated interferon (PEG-IFN) plus ribavirin, which in clinical trials have shown a moderate efficacy unfortunately with many adverse effects. The sustained virologic response (SVR) rates were 40 to 50%.[1,2] At that time, first-in-class protease inhibitors [(PIs) (boceprevir and telaprevir)] were the first direct-acting antiviral (DAA) therapies approved for patients with GT1, given in conjunction with both PEG-IFN and ribavirin for a total of 24 to 48 weeks, depending on whether the patient had a robust response (ranged from 63 to 75%).[3,4] Fortunately, with the development of the second wave of DAA which are specifically designed to target HCV proteins, particularly the non-structural proteins, there are new therapies available. In fact, the efforts have focused on the six nonstructural (NS) proteins (NS2, NS3, NS4A, NS4B, NS5A, and NS5B) that play critical roles in HCV entry, replication, and proliferation and will serve as possible targets for the development more DAA therapies.

The good of the DAA is that they can reduce the length of antiviral treatment, improve response rates, and allow for interferon-free regimens for some HCV genotypes.

On the other hand, the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) offers two options for interferon (IFN)-neligible/intolerant individuals with GT1 infection: sofosbuvir/ribavirin (SOF/RBV) for 24 weeks or sofosbuvir/simeprevir (SOF/SMV) for 12 weeks. A 24-week course of SOF/RBV costs approximately US$169,000, with SVR rates ranging from 52% to 84%; 12 weeks of SOF/SMV costs approximately $150,000, with SVR between 89% and 100%.

Hogan, *et al*.[5] have analyzed the cost effectiveness of these two treatment regimens accounting for costs of drugs, treatment-related medical care, retreatment for individuals who do not achieve SVR, and natural history of continued HCV infection after failed retreatment. Those investigators found that SOF/SMV yielded lower costs and more quality-adjusted life years (QALYs) for the average subject, compared to SOF/RBV ($165,336 and 14.69 QALYs *vs*. $243,586 and 14.45 QALYs, respectively). In base-case cost analysis, the SOF/SMV treatment strategy saved $91,590 per SVR, compared to SOF/RBV.

The results of this study suggest that the combination of SOF/SMV for 12-week is a more cost-effective treatment for GT1- HCV patients. There is no question that DAA improve response rate of treatment.

The bad or disadvantage is that these new agents have a high cost and are not available in different areas of the world. In fact, numerous non-governmental organizations and government agencies are conducting cost effectiveness studies in order to spread the treatments. For example, the pharmaceutical company has made an agreement

Correspondence and reprint request: Prof. Nahum Méndez-Sánchez, MD, MSc, PhD, FACG, AGAF.
Liver Research Unit, Medica Sur Clinic & Foundation
Puente de Piedra, 150. Col. Toriello Guerra, Mexico City, Mexico.
Tel.: +5255 5424-7200 (4215). Fax: +5255 5666-4031
E-mail: nmendez@medicasur.org.mx

Manuscript received: July 27, 2014.
Manuscript accepted: July 27, 2014.

with health authorities in Egypt to make SOF available (US$1000) in a country where the prevalence on HCV is extremely high.

The ugly is that the later strategy, pharmaceutical companies-government, is not easy to achieve all over the world, especially in the so called low and middle income countries, where the prevalence of HCV is high and the health systems are unable to cover all the population. Moreover, public politics in many countries have acted as barriers for the supplementation of these medications, in Latin America as an example, there is not currently any pharmaceutical company producer of DAA involved in such strategy, which is surprising given the number of people affected.[6,7] **Even more ugly** is the fact that looking to the future, solutions are not easy to achieve, there are many challenges in this field.

What can we suggest at this time in emergent countries? First HCV must be recognized as an important public health problem, its natural history must be taken into account and increase the screening in general population, we cannot wait until the disease produces signs and symptoms, since for many patients this could be too late and for the health systems too costly.

HCV is a complex and increasing problem, where the whole society has to be involved. The health professionals must be aware of patients with liver risk factors and send them for HCV screening, it is urgent to have better public health surveillance strategies; health systems must understand the need of cover the medication demand for patients who already have a HCV diagnosis; health insurances also must be prepared to face this health problem and last but not least the pharmaceutical companies must understand that the high prices of these medications cannot be paid in many countries.

REFERENCES

1. Geneva: Hepatitis C fact sheet. In: World Health Organization, 2012.
2. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology* 2013: 57: 1333-42. doi: 10.1002/hep.26141.
3. Poordad F, McCone J, Jr., Bacon BR, Bruno S, Manns MP, Sulkowski MS, Jacobson IM, et al. Boceprevir for untreated chronic HCV genotype 1 infection. *N Engl J Med* 2011: 364: 1195-206. doi: 10.1056/NEJMoa1010494.
4. Jacobson IM, McHutchison JG, Dusheiko G, Di Bisceglie AM, Reddy KR, Bzowej NH, Marcellin P, et al. Telaprevir for previously untreated chronic hepatitis C virus infection. *N Engl J Med* 2011: 364: 2405-16. doi: 10.1056/NEJMoa1012912.
5. Hagan LM, Sulkowski MS, Schinazi RF. Cost analysis of sofosbuvir/ribavirin versus sofosbuvir/simeprevir for genotype 1 hepatitis C virus in interferon-ineligible/intolerant individuals. *Hepatology* 2014: 60: 37-45. doi: 10.1002/hep.27151.
6. Mendez-Sanchez N. The socioeconomic impact of hepatitis C infection and liver transplantation in Mexico. *Ann Hepatol* 2012: 11: 550-1.
7. Szabo SM, Bibby M, Yuan Y, Donato BM, Jimenez-Mendez R, Castaneda-Hernandez G, Rodriguez-Torres M, et al. The epidemiologic burden of hepatitis C virus infection in Latin America. *Ann Hepatol* 2012: 11: 623-35.