

**DIRECT- ACTING ANTI- HEPATITIS C AGENTS AND THE RISK OF  
HEPATOCELLULAR CARCINOMA DEVELOPMENT VS THE OLD AGENTS: DOES  
THE OLD STILL THE GOLD?**

Erwa Elmakki\*

Assistant Professor, Department of Internal Medicine, Faculty of Medicine, Jazan University, Kingdom of Saudi Arabia.

**\*Corresponding Author: Erwa Elmakki**

Assistant Professor, Department of Internal Medicine, Faculty of Medicine, Jazan University, Kingdom of Saudi Arabia.

Article Received on 14/07/2017

Article Revised on 03/08/2017

Article Accepted on 24/08/2017

Direct acting anti-viral (DAA) are the newest medications used for treatment of Chronic hepatitis C (CHC). DAA agents were approved by the American Food and Drug Administration (FDA) in 2014 as a novel treatment for CHC.<sup>[1]</sup> Commonly used DAA regimens include: Sofosbuvir plus Simeprevir or Ledipasvir for hepatitis C virus (HCV) genotype 1, and Sofosbuvir plus Velpatasvir for all HCV genotypes.<sup>[1]</sup>

Before the year 2011, treatment of CHC was consisted of a combination of pegylated interferon alpha and Ribavirin for duration of 24 or 48 weeks, depending on HCV genotype. This produces cure rates of between 70 and 80% for genotype 2 and 3, respectively, and 45 to 70% for genotypes 1 and 4. Adverse effects with these treatments were common, with half of the people getting flu like symptoms and a third experiencing emotional problem.<sup>[2]</sup> However, many studies have demonstrated the lower rates of hepatocellular carcinoma (HCC) in patients treated with interferon-based regimens.<sup>[3]</sup> On the other hand, DAA agents are more effective in terms of achieving very high Sustained virological response (SVR) rates, ranging from 95-99%. In addition to that, DAA agents are well tolerated, safe, given in short duration and they are effective for all HCV genotypes.<sup>[4]</sup> However, based on recent reports there has been much concern in the high incidence of HCC and recurrence rates of HCC with the use of DAA agents especially in those who achieved SVR.<sup>[5,6]</sup> To date, no solid evidences to explain the higher rates of HCC in those treated with DAA agents, as the majority of the studies which reported such relation were primarily designed for assessing the DAA effect on CHC treatment and not for long-term impact on the natural history of the disease. No doubt, further large multi center, randomized control trials are needed in order to assess such relation. For the time being, some questions need to be answered: is there any emergence to change our current practice in terms of HCC surveillance? Also shall Interferon-based regimen be introduced in CHC patients at higher risk of HCC?

**CONFLICT OF INTEREST**

The author declares that no conflict of interest and no direct financial relationship to the work presented.

**REFERENCES**

1. 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 randomized study. *Lancet*, 2014; 15(384): 1756-65.
2. Michielsen P, Ho E, Francque S, et al. Does antiviral therapy reduce the risk of hepatocellular carcinoma in patients with chronic hepatitis C? *Minerva Gastroenterol Dietol*, 2012; 58: 65-79.
3. Hsu S, Chao C, Lin HH, et al. Systematic Review: Impact of Interferon-based Therapy in HCV-related Hepatocellular Carcinoma. *Scientific Reports*, 2015; 5: 9954.
4. Falade O, Suarez C, Nelson DR, et al. Oral Direct-Acting Agent Therapy for Hepatitis C Virus Infection: A Systematic Review. *Ann Intern Med*, 2017; 166. doi: 10.7326/M16-2575.
5. Ravi S, Axley P, Jones D, et al. Unusually High Rates of Hepatocellular Carcinoma After Treatment With Direct-Acting Antiviral Therapy for Hepatitis C Related Cirrhosis. *Gastroenterology*, 2017; 152: 911-912.
6. Baumert T, Juhling F, Ono A, et al. "Hepatitis C-Related Hepatocellular Carcinoma in the Era of New Generation Antivirals." *BMC Medicine*, 2017; 15: 52.