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Letter to Editor
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Occurrence and Recurrence of Hepatocellular Carcinoma after Direct-Acting Antiviral Therapy: A Truth or a Myth?

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Letter to Editor

Chronic Hepatitis C (CHC) is a global health epidemic affecting more than 70 million people worldwide. More than 80% of CHC patients will progress to liver cirrhosis, of which about 20% will eventually develop Hepatocellular Carcinoma (HCC) [1].

During the previous decades, treatment of CHC depended on interferon-ribavirin combination with Sustained Virologic Response (SVR) less than 50% in most centers. Emergence of Direct Acting Antiviral (DAAs) drugs five years earlier provided a significant improvement in SVR achievement (more than 95%) in most centers and studies [2].

Reig et al. and other studies recently raised a global concern regarding increased de novo and recurrence of HCC following DAAs [3].

However, their studies had many points of criticism including inappropriate or not-fully elucidated criteria for selecting patients, their studies, timing of initiating DAAs treatment after HCC treatment, statistical bias, few numbers of patients in their studies etc [4].

Depending on the available meta-analysis studies, DAAs are not considered carcinogenic although they lack the anti-carcinogenic effect of INF. However, many authors still have reasonable concerns regarding the hepatic biochemical and immunological responses to CHC eradication after DAAs especially in patients with decompensated cirrhosis. Eradication of HCV after DAAs may change the types of immunological cells and cytokines in the liver, which in turn may pave the way for the abnormal proliferation of liver cells in those patients [5].

The timing for DAAs initiation after successful treatment of HCC, which must be at least 4-6 months, seems to be important in reducing HCC recurrence after DAAs therapy. Also, meticulous follow up is warranted in patients with cirrhosis who received DAAs because cirrhosis itself is the most common risk factor for HCC regardless of the underlying aetiology or DAAs use [6].

Improvement of the clinical, biochemical and histological features of chronic liver disease after DAAs therapy especially in cirrhotic patients provides higher success rates of the de-novo or recurrent HCC treatment with Radiofrequency Ablation (RFA), Trans-Arterial Chemoembolization (TACE) or surgical resection [7].

We conducted a multicenter study included 321 patients with CHC. One-hundred fifty patients were non-cirrhotic, 171 patients were cirrhotic of which 116 patients without previous history of HCC and 55 patients had a history of HCC and received DAAs after at least 6 months of successful HCC treatment. All patients received the same regimen of DAAs (Sofosbuvir and Daclatasvir +/- ribavirin) for 12 weeks. The SVR was 100% in non-cirrhotic patients and 91% in cirrhotic patients. After a median follow up period of 12 months for all patients whether achieved SVR or not, Only 6 patients had de-novo HCC, all were from the cirrhotic group, (1.9% of all patients & 5.2% of cirrhotic patients without previous HCC) and 9 patients had recurrent HCC (2.8% of all patients & 16.4% of cirrhotic patients with previous HCC).

Univariate and multivariate analysis showed that cirrhosis, previous multifocal HCC and persistent ALT elevation after SVR achievement were the most important risk factors for HCC Occurrence and recurrence after DAAs. Our findings suggest no role for DAAs in occurrence or recurrence of HCC after CHC eradication.

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