Study of the early occurrence of hepatocellular carcinoma (HCC) in Egyptian HCV infected patients receiving Sofosbuvir and Daclatasvir

Introduction:

Hepatitis C virus (HCV) is a major public health problem. Up to 25% of chronically infected patients eventually develop cirrhosis and related complications, including hepatocellular carcinoma. The goal of HCV treatment is to eradicate the virus and prevent the development of cirrhosis and its complications. Successful treatment of HCV has been defined in terms of sustained virologic response (SVR), which is the absence of detectable levels of viral RNA in the blood 24 weeks after completion of therapy (Jazwinski ,et al; 2011).

Chronic infection with hepatitis C virus (HCV) occurs in roughly 180 million people worldwide, and although genotype 1 accounts for roughly 48% of infections, distribution of the seven genotypes differs geographically. Genotype 4 infections account for 13–20% of all HCV infections worldwide, but make up about 93% of all HCV cases in Egypt. HCV is epidemic in Egypt since seroprevalence has been reported in more than 10% of Egyptians (8 million individuals), which is substantially higher than in other geographic regions, and an estimated 7–10% of Egyptians are chronically infected. New direct-acting antiviral treatment options for HCV have mainly focused on treatment of patients with genotype 1 infection because of the high worldwide prevalence of this genotype and because it has historically

been difficult to cure with interferon-based regimens. Some direct-acting antiviral regimens have shown activity against several genotypes and future regimens have the potential to be pangenotypic. However, few dedicated studies with these new regimens have been done in patients with HCV genotype 4 infection, especially in Egyptian patients, who make up 35–45% of the global pool of genotype 4 infection (waked, et al; 2016).

The pegylated interferon regimen has long been the lonely effective management of chronic hepatitis C with modest response. The first appearance of protease inhibitors included boceprevir and telaprevir. However, their efficacy was limited to genotype 1. Recently, direct antiviral agents opened the gate for a real effective management of HCV, certainly after FDA approval of some compounds that further paved the way for the appearance of enormous potent direct antiviral agents that may achieve successful eradication of HCV (Esmat, et al; 2014).

Direct-acting antiviral agents (DAAs) are a major breakthrough in the management of HCV and to prevent progressive liver disease. Assessment of HCC incidence and risk factors following sustained virological response (SVR) are important to prioritize patients for HCC surveillance in the era of highly effective DAAs, when many patients with advanced fibrosis and cirrhosis who were not previously treated are now being treated. However,

there is limited data available on the effect of SVR from interferon-based treatments on HCC risk, long term HCC incidence post SVR and determinants of HCC post SVR. Evidence is especially limited on HCC risk post SVR among those with advanced fibrosis to recommend optimal post SVR follow-up for HCC. Available data has mainly been derived from small studies or studies from Asia, most with short duration of follow-up to assess HCC risk post SVR (Janjua, et al; 2016).

Patients with HCV-related cirrhosis, DAA induced resolution of HCV infection does not seem to reduce the occurrence of HCC, in the short term. In addition, patients previously treated for HCC have still a high risk of tumour recurrence, despite DAA treatment. For these reasons, all cirrhotic patients should be closely monitored, during and after antiviral therapy, implementing or continuing HCC surveillance, despite resolution of HCV infection (Conti, et al; 2016)

Aim of the study:

To evaluate the early detection of HCC in patients Taking Sofosbuvir and Daclatasvir.

Methodology:

- **Design:**

Prospective, randomized study used to detect early incidence of HCC in patients taking Sofosbuvir and Daclatasvir to treat HCV.

100 patients will be recruited from the National Hepatology and Tropical Medicine Research Institute (NHTMRI) with the following criteria

- **Inclusion criteria:**

  - 100 Patients have positive HCV-RNA and taking DAAS to treat it.
  - Both sexes will be included
  - Age above 18 to 75 years old
  - Child Pugh score (A and B)

- **Exclusion Criteria:**

  - Total serum bilirubin>3 mg/dl
  - Serum albumin < 2.8 g/dl
  - INR≥ 1.7
  - Platelet count< 50000/mm3

IF any of the above criteria is not caused by liver disease, the patient can be included in the study.

- HCC, except 4 weeks after intervention aiming at cure with no evidence of activity by dynamic imaging (CT or MRI).
- Extra- hepatic malignancy.
- Pregnancy or inability to use effective contraception.
- Inadequately controlled diabetes mellitus (HbA1c>9%).

➢ **Duration of study:**

24 weeks from starting the DAAs

➢ **Methods:**

➢ **Patients will go through examination and lab. Workup three times in this study:** (Bruix J., et al. 2016)

- **FIRST Visit:**
  - Before starting antiviral therapy, all included patients will undergo through physical examination, lab workup including HCV-RNA quantitative, fasting plasma glucose or HbA1C if diabetic, serum creatinine, CBC, AST, ALT, prothrombin Concentration or INR, total bilirubin, serum albumin, Pregnancy test (Ladies in child bearing period), AFP as a marker of HCC.
  - Included patients will also undergo through diagnostic procedures as Abdominal ultrasonography and ECG (men >40, women>50).

- **Second visit**:

    - At the end of antiviral therapy (12 weeks), virological response to therapy will be assessed by quantitative HCV RNA detection, using PCR.
    - Patients will lab workup including , fasting plasma glucose or HbA1C if diabetic, serum creatinine, CBC, AST, ALT, prothrombin Concentration or INR, total bilirubin, serum albumin, AFP as a marker of HCC.
    - The abdominal ultrasonography will be repeated any suspected focal lesion of the liver will be evaluated with triphasic CT scan or MRI to assess the occurrence or the recurrence of HCC.

- **Third and last visit:**
    - At 24 weeks (Patients will be off treatment for the previous 12 weeks) , virological response to therapy will be assessed by quantitative HCV RNA detection, using PCR.
    - Patients will lab workup including , fasting plasma glucose or HbA1C if diabetic, serum creatinine, CBC, AST, ALT, prothrombin Concentration or INR, total bilirubin, serum albumin, AFP as a marker of HCC.

- The abdominal ultrasonography will be repeated any suspected focal lesion of the liver will be evaluated with triphasic CT scan or MRI to assess the occurrence or the recurrence of HCC.

- **Statistical Analysis:**

- According to the data results; T test, Chi square, and/ or ANOVA will be used to analyze the results using SPSS

References

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