بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

MONA MAGHRABY

Recurrence Rate of Hepatocellular Carcinoma after Treatment of Chronic Hepatitis C Patients with Direct Acting Antivirals: Randomized Controlled Phase 3 Trial (Cautious Trial)

Thesis

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Fatma Sayed Mohamed Abdelbakey

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List of Abbreviations

Abb.	Full term
A1ATD	α1-Antitrypsin deficiency
AASLD	American Association for the Study of Liver Diseases
AFB1	Aflatoxin B1
AFP	Alpha-fetoprotein
AGA	American Gastroenterology Association
AHPBA	Americas Hepato-Pancreato-Biliary Association
AIH	Autoimmune hepatitis
AJCC	American Joint Committee on Cancer
ALBI	Albumin-bilirubin
ASIRS	Age-standardized incidence rates
BCLC	Barcelona Clinic Liver Cancer
CECT	Contrast-enhanced computed tomography
CEMRI	Contrast-enhanced magnetic resonance imaging
CEUS	Contrast-enhanced US
CI	Confidence interval
CLIP	Cancer of the Liver Italian Program
CT	Computed tomography
DAA	Direct-acting antiviral
EASL	European Association for the Study of the Liver
EGFR	Epidermal growth factor receptor
EOT	End of therapy
FDG-PET	Fluorodeoxyglucose-positron emission tomography
GALC	German Alliance for Liver Cancer

List of Abbreviations cont...

Abb.	Full term
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HLA	Human leukocyte antigen
HR	Hazard ratio
IBT	Interferon based therapy
ICC	Intrahepatic cholangiocarcinoma
IFN	Interferon
IGF-1	Insulin like growth factor-1
IL	Interleukin
IRE	Irreversible electroporation
JIS	Japanese Integrated Staging
LI-RADS	Liver Imaging Reporting and Data System
LMICs	Lower-middle income countries
LOD	Limit of detection
mRECIST	Modified Response Evaluation Criteria in Solid Tumors
MRI	Magnetic resonance imaging
MSM	Men who have sex with men
MWA	Microwave ablation
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
ORR	Objective response rate
OS	Overall survival
PS	Performance status
PWID	People who inject drugs
rCR	Radiological complete response
RFA	Radiofrequency ablation

List of Abbreviations cont...

Abb.	Full term
RFS	Recurrence-free survival
RR	Recurrence Rate
SVR	Sustained virological response
TACE	Trans-arterial chemoembolization
TKI	Tyrosine kinase inhibitors
TNM	Tumor, Node, Metastasis
TTR	Time to recurrence
UICC	Union for International Cancer Control
UNOS	United Network for Organ Sharing
WHO	World health organization

INTRODUCTION

Hepatocellular carcinoma (HCC) represents about 75–85% of primary liver cancers [(1)], it is the sixth most common cancer and the third leading cause of cancer-related death worldwide [(2)]. Whereas in Egypt, it represents the most commonly diagnosed cancer, with about 27,895 new case in 2020 [(3)], a consequence of the high prevalence of hepatitis C virus (HCV) infection in Egypt [(4)], with an estimated 10% of the total population were seropositive for HCV antibodies and 7% had viremia as reported in the Egyptian Demographic and Health Survey (DHS) of 2015, what constitutes a major health and economic burden [(5)].

HCV genotype 4 is considered the most predominant genotype in Egypt [(6)], with about 10–20% of individuals with chronic HCV infection has complications, including decompensated cirrhosis and HCC, over a period of 20–30 years [(7)]. When liver cirrhosis is established, the 5-year risk of HCC occurrence is approximately 13% in those with cirrhosis [(8)]. However, our map and records of HCV, and viral hepatitis in general, have recently some changes owing to the immigration to Egypt after revolutions and wars in the Middle Eastern countries in the recent years, so screening for immigrants regarding the HCC risk factors, in general, and both Hepatitis B virus (HBV) and HCV, in particular, should be encouraged [(9)].

With the introduction of the direct-acting antiviral (DAA) agents in 2014 as an effective HCV treatment, the National Committee for Control of Viral Hepatitis (NCCVH) started a national program to make HCV treatment available for all and covered by the Egyptian government [10], therefore, by 2018 40% of the total HCV-infected population were treated (about more than 2 million patients), with sustained virological response (SVR) rate above 90% [4]. This in line with the World health organization (WHO) global hepatitis strategy to eradicate viral hepatitis by 2030 [11].

Chronic HCV patients with prior history of HCC was a challenging situation in HCV treatment, our NCCVH recommended to receive DAA after more than 4 weeks of HCC treatment and achieving radiological complete response (rCR) [12]. Although many studies proved reduced HCC occurrence and recurrence after interferon based therapy (IBT), it was unclear if this the same benefit would be seen with DAAs [13].

Early reports showed high HCC recurrence rate (RR) after DAA in chronic HCV patients with prior history of DAA [14–23], which followed by other studies reported contradictory results that DAA did not increase the HCC recurrence [24–33], meanwhile some studies revealed that DAA associated with decrease HCC RR [34–41].

Therefore, a constant debate is still ongoing and the evidence is yet unclear whether DAA therapy may increase