Clinical outcome of Simeprevir Plus Sofosbuvir Regimen in Comparison to Daclatasvir Plus Sofosbuvir Regimen for Treatment of Chronic Hepatitis C Egyptian Cirrhotic and Non-cirrhotic Patients

Thesis

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Abstract

Introduction: Hepatitis C is an infectious disease caused by hepatitis C virus (HCV) which mainly attacks the liver cells**.** The acute stage of the disease passes mostly without manifestations, but the chronic stage can cause hepatic fibrosis and cirrhosis, that has mostly occurred after several years. Some cirrhotic patients may develop liver failure, hepatocellular carcinoma (HCC) or fatal bleeding from esophageal or gastric varices.

Aims: The aim of this study is to compare between the clinical outcome of Simeprevir plus Sofosbuvir regimen and Daclatasvir plus Sofosbuvir regimen in the management of Treatment-naïve chronic Hepatitis C Egyptian patients with compensated cirrhosis and non-cirrhotic patients as regards to sustained virological response (SVR) at the end of treatment and 12 weeks after the end of treatment and the clinical data till the end of the treatment.

Patients and Methods: This study has been conducted at the Viral Hepatitis Unit – Ahmed Maher Teaching Hospital – National committee for the control of viral hepatitis (NCCVH) during the period from June 2015 to November 2016.

Results: 400 Egyptian treatment-naïve chronic hepatitis C patients were recruited in this study and were divided into 2 groups:

Group I: 200 patients received fixed daily dose (400mg Sofosubvir +150mg Simeprevir) for 12 weeks.

Group II: 200 patients received fixed daily dose (400mg Sofosubvir +60mg Daclatasvir) for 12 weeks.

Conclusion: Both (simeprevir plus sofosbuvir) and (daclatasvir plus sofosbuvir) oral regimens for treatment of chronic HCV infected patients with or without compensated cirrhosis are effective and well tolerated, with non-significant difference between them.

Recommendation: Both (simeprevir plus sofosbuvir) and (daclatasvir plus sofosbuvir) oral regimens for 12 weeks are good options in the treatment of chronic HCV infected patients with or without compensated cirrhosis. Careful monitoring of CBC, liver enzymes, serum bilirubin and serum creatinine during treatment.

Keywords: Simeprevir Plus, Sofosbuvir Regimen Daclatasvir Plus Sofosbuvir, Treatment of Chronic Hepatitis C

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Contents

List of Abbreviations

Abbreviation	Meaning
AFP	Alpha feto-protein
Ag	Antigen
ALT	Alanine aminotransferase
APRI	AST/ Platelet ratio index
ARFI	Acoustic radiation force impulse
AST	Aspartate aminotransferase
AUC	Area under the curve
bDNA	branched deoxyribonucleic acid
BMI	Body mass index
CBC	Complete blood count
CDC	Centers for disease control and prevention
CHC	Chronic hepatitis c
CLD	Chronic liver disease
CLIA	Chemi-luminescence immunoassay
CNS	Central nervous system
CTGF	Connective tissue growth factor
CTP	Child-Turcotte-Pugh Classification system
DAAs	Direct acting antiviral agents
DCV	Daclatasvir
DM	Diabetes mellitus
EASL	European association for the study of the

	liver
EBR	Elbasvir
ECM	Extracellular matrix
ELF	Enhanced liver fibrosis
eGFR	estimated glomerular filtration rate
EIA	enzyme immunoassay
ELISA	Enzyme-linked immunosorbent assay
ESRD	End stage renal disease
ETR	End of treatment response
EVR	Early virologic response
GGT	Gamma-glutamyl transferase
GZR	Grazoprevir
HA	Hyaluronic acid
HBV	Hepatitis b virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis c virus
HFL	Hepatic focal lesion
HIV	Human immunodeficiency virus
HSC	Hepatic stellate cells
IG	Immunoglobulin
IgG	Immunoglobulin G
IRES	Internal ribosome entry site
ISGs	Interferon stimulated genes
IU	International unit

LDL	Low density lipoproteins
LDL-R	Low density lipoproteins receptor
LDV	Ledipasvir
MELD	Model for End-Stage Liver Disease
MFAP-4	Microfibril-associated glycoprotein 4
MMPs	Metalloproteinases
MRE	Magnetic Resonance Elastography
Mrna	Messanger RNA
NAFLD	Non-alcoholic fatty liver disease
NAT	Nucleic acid test
NCCVH	National committee for the control of viral hepatitis
OELF	Original European Liver Fibrosis
PICP	Procollagen type I carboxy terminal peptide
PIIINP	Procollagen type III amino-terminal peptide
PBMCs	Peripheral blood mononuclear cells
PCR	Polymerase chain reaction
Peg IFN	Pegylated interferon
PWIDs	People who inject drugs
qRT-PCR	quantitative Reverse transcriptase polymerase chain reaction
RBCs	Red blood cells
RBV	Ribavirin
RIBA	Recombinant immunoblot assays
RNA	Ribonucleic acid

RT-PCR	Reverse transcriptase polymerase chain reaction
RVR	Rapid virological response
Sim	Simeprevir
SOF	Sofosbuvir
SVR	Sustained virological response
TGF-β1	Transforming growth factor-β1
TIMPs	Tissue inhibitors of matrix metalloproteinases
TMA	Transcription-mediated amplification
U/S	Ultrasound
US	United states
UTR	Untranslated region
VEL	Velpatasvir

List of Figures

List of Tables

Introduction

Hepatitis C is an infectious disease caused by hepatitis C virus (HCV) which mainly attacks the liver cells **(Yu et al., 2007).** The acute stage of the disease passes mostly without manifestations, but the chronic stage can cause hepatic fibrosis and cirrhosis, that has mostly occurred after several years. Some cirrhotic patients may develop liver failure, hepatocellular carcinoma (HCC) or fatal bleeding from esophageal or gastric varices **(Springer, 2011).**

It is estimated that up to 170-200 million people (3% of the world population) have chronic HCV infection. All over the world, about 350,000 people die each year due to HCV related chronic liver disease **(Lavanchy, 2009).**

Egypt has the highest prevalence rate of HCV in the world. About 14.7% of the Egyptian people have HCV antibodies **(Esmat, 2013)** and 9.8% have an active infection **(El Zanaty et al., 2009).**

With the ultimate goal of achieving a more potent strategy to control transmission of HCV in Egypt, The Ministry of Health has set up 32 specialized centers for the