Study the Response of Qurevo (Ombitasvir, Paritaprevir and Ritonavir)

in End Stage Renal Disease Patients with Hepatitis C Virus

Thesis

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

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CONTENTS

List of abbreviations

Abb.	Full Term
24 W	24 Weeks
48 W	48 weeks
AAMI	Association for the Advancement of Medical Instrumentation
AASLD	American Association for the Study of Liver Diseases
AE	Adverse events
ALT	Alanine aminotransferase
Anti-C5 antibody	Anti C5 convertase /Monoclonal antibody
ART	Association of Renal Technologists
AST	Aspartate aminotransferase
AVF	Arterio venous fistula
AVG	Arterio venous graft
bDNA	Branched deoxyribonucleic acid
BSI	Bloodstream Infection
C1q	Complement 1 q
C2 ,C4 deficiency	Complement 2, complement 4 deficiency
CD 20	B-lymphocyte antigen CD20
CD81	Cluster of differentiation 81
CDC	Centers for disease control and prevention
CFU	Colony Forming Unit
CH50	Complement hemolytic activity
CI	Confidence interval
CKD	Chronic kidney disease
CLD	Chronic liver disease
CMV	Cytomegalo virus
CT	Computed tomography
CYP2D6	Cytochrome P450 2D6
CYPD6	Cytochrome P450 family 2 subfamily D member 6
D77	Day 77
DAA	Direct -acting anti viral agents
DM	Diabetes mellitus
DOPPS	Dialysis outcomes and analysis of practice patterns
DSV	Dasabuvir
E1	Envelope glycoprotein 1

List of Abbreviations (cont…)	
E2	Envelope glycoprotein 2
EASL	European Association for the Study of the Liver
EIA	Enzyme immunoassay
ELISA	Enzyme Linked Immunosorbent Assay
ESRD	End stage renal disease
EU/ml	Endotoxin units per milliliter
F0,F1,F2,F3	Fibrosis stage
Fulm.	Fulminant
GFR	Glomerular filteration rate
GIT	Gastrointestinal tract
GN	Glomerulonephritis
GT	Genotype
Hb/HGB	Hemoglobin
HbA1c	Glycosylated hemoglobin
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HD	Hemodialysis
HFE gene	High Iron Fe /hemochromatosis gene
HIV	Human immune-deficiency virus
HUS	Hemolytic uremic syndrome
IAS-USA	International Accounting Standards-United states of america
IDSA	Infectious Diseases Society of America
IFN	Interferon
IgA	Immunoglobulin A
IGF-1	Insulin like growth factor -1
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IL 28 B cc	Interleukin 28 B cc
IL6	Interleukin 6
IL8	Interleukin 8
INR	International normalised ratio
IRES	Internal ribosome entry site
ITT	Intention-to-treat
IV	Intravenous
KDOQI	Kidney Disease Outcomes Quality Initiative

List of Abbreviations (cont…)	
LKM1	Anti-kidney microsome type 1
mITT	Modified intention to treat
MHD	Maintenance hemodialysis
MPGN	Membranoproliferative Glomerulonephritis
MRI	Magnetic resonance imaging
MRSA	Methicillin-resistant Staphylococcus aureus
n	Number
NAT	Nucleic acid testing
NHANES	The National Health and Nutrition Examination Survey
NHL	Non-Hodgkin lymphoma
NHT	Normal hematocrit trial
NS 3	Non structural protein 3
NS 5A	Non structural protein 5 a
NS2	Non structural protein 2
NS4A	Non structural protein 4 A
NS4B	Non structural protein 4 B
NS5B	Non structural protein 5 B
OBV	Ombitasvir
P	Prevelance
P7	Polyprotein 7
PAS	Periodic Acid-Schiff
PCR	Polymerase chain reaction
PDRA	Pan-Drug-Resistant Acinetobacter
Peg interferon	Pegylated interferon
PI	Protease inhibitor
PLD	Partial lipodystrophy
Plt	Platelets
PPE	Personal protective equipment
PTV	Paritaprevir
QA/QI	Quality Assessment and Quality Improvement
r	Ritonavir
RBV	Ribavirin
RNA	Ribonucleic acid
RR	Relative risk
RT	Reverse transcription
S.	Serum
SLE	Systemic lupus erythematosus

List of Abbreviations (cont…)	
SOCS3	Suppressor of cytokine signaling 3
SOF	Sofosbuvir
SRBI	Scavenger receptor class B type 1
SVR	Sustained virologic response
TGF-B	Transforming growth factors beta- 1
TIW	Three times a week
TLR3	Toll –like receptors 3
TMA	Transcription mediated amplification
TTP	Thrombotic thrombocytopenic purpura
UK	United kingdom
VRE	Vancomycin-resistant Enterococci
W2	Week 2
WHO	World health organization

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INTRODUCTION

Persons infected with hepatitis C virus(HCV) can develop kidney disease as a result of extrahepatic manifestation of HCV or as a disease process independent of the HCV infection. In addition, hemodialysis has been a risk factor for acquiring HCV infection . Several studies have shown that patients on chronic hemodialysis have an increased overall mortality risk if they have chronic hepatitis C infection (when compared with those on dialysis who do not have hepatitis C infection). There are some data showing that chronic hepatitis C may be a risk factor for developing renal cell carcinoma. Chronic hepatitis C infection has also been associated with an accelerated course of renal disease in HIV-infected persons. Extrahepatic manifestations related to HCV, including immune complex-related renal disease, can require urgent HCV treatment to resolve or prevent further organ damage***(Fabrizi et al., 2014)***

The availability of new direct-acting antiviral agents (DAAs) has sparked major enthusiasm for treating HCV-infected patients with renal impairment. The following summarizes key studies involving use of new DAA based therapy in patients with chronic renal insufficiency. Investigators treated HCV-infected patients with stage 4 or 5 renal disease, including patients on hemodialysis, with a 12-week regimen of Qurevo with or without ribavirin. All patients enrolled in the initial phase had genotype 1 chronic HCV infection, were treatment-naïve, and had noncirrhotic liver disease. In the preliminary analysis, 10 (100%) of 10 treated patients achieved a sustained virologic response 4 weeks after completion of therapy (SVR4) and no treatment related serious adverse events occurred. ***(Messa and Fabrizi, 2015)***

Previous study in 2016 showed that twelve weeks of Qurevo achieved sustained viral response in 90% of patients with non-cirrhotic chronic hepatitis C virus (HCV) genotype 1 infection and comorbid stage 4 or 5 chronic kidney disease, according to a small, single-arm, industry-sponsored trial reported in the November issue of Gastroenterology. Adverse effects were usually mild or moderate, and serious adverse effects were considered unrelated to treatment . No patients stopped direct-acting antivirals because of adverse effects, although nearly half had to interrupt or discontinue ribavirin because of worsening anemia. The results of this study are important to initiate the direct-acting antiviral therapy in HCV-infected patients with end-stage renal disease and also to prevent end-stage sequelae of HCV. ***(Janssen et al., 2016)***