

Trial of New Antiviral Drugs in Patients
With Decompensated Liver Cirrhosis
Due to HCV Infection

Thesis

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Summary

Egypt has the largest burden of Hepatitis C virus in the world, the overall prevalence for positive HCV Ab in Egypt was 14.7%. 9.8% of the population continues to have HCV RNA, which means that 7.8 millions of the Egyptians continue to have chronic active hepatitis (According to Egyptian demographic health survey) (*Kamel et al., 1992*).

Cirrhosis represents the end stage of any chronic liver disease, it can remain compensated for many years prior to development of decompensating events; decompensated cirrhosis is marked by the development of jaundice, variceal hemorrhage, ascites or encephalopathy (*Sakib and Garcia-Tsao., 2003*).

According to the NIH Consensus Conference Statement, the primary therapy recommended for patients with decompensated liver disease due to HCV infection is referral for liver transplantation (*National Institute Of health consensus development conference statement, 2002*).

Interferon and ribavirin therapy (the standard antiviral therapy for HCV infection) is potentially dangerous in the setting of decompensated cirrhosis because of the increased risk of life threatening complications and because of the concern that it might accelerate hepatic decompensation (*Crippen et al., 2002*).

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List of Abbreviations

aa	Amino Acid
AASLD	American Association For The Study Of Liver Disease
AFP	Alpha Fetoprotein
AFP-L3	Lens Culinaris Agglutinin-Reactive AFP
Ag	Antigen
AIDS	Acquired Immune Deficiency Syndrom
AKI	Acute Kidney Injury
AP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferases
AT	Antithrombin
BMI	Body Mass Index
CD4	Cluster Of Differentiation 4
CD 81	Cluster Of Differentiation 81 (Target Of Anti Proliferation Antibody)
CHC	Chronic Hepatitis C
Cr Cl/min	Creatinine Clearance Per Minute
CTP	Child –Turcotte -Pough
CT	Computed Tomography
DAA	Direct-Acting Antiviral Agent
D. Bil	Direct Bilirubin

DC-SIGN	Dendritic Cell-Specific Intercellular Adhesion Molecule-3-Grabbing Nonintegrin
DCP	Desgamma Carboxy Prothrombin
DNA	De-Oxy Ribonucleic Acid
DVR	Delayed Virological Response
E1	Envelope Protein 1
E2	Envelope Protein 2
ECM	Extra Cellular Matrix
EDHS	Egyptian Demographic Health Survey
EIF	Eukaryotic Translation Initiation Factor
EIA	Enzyme Linked Immunosorbent Essay
ER	Endoplasmic Reticulum
EVR	Early Virologic Response
FDA	Food And Drug Administration
G-CSF	Granulocyte Colony Stimulating Factor
GGT	Gamma Gluteryl Transferase
GH	Growth Hormone
GM-CSF	Granulocyte Macrophage Colony-Stimulating Factor
Gpc 3	Glypican 3
GTP	Guanosin Triphosphate
HBeAg	Hepatitis B E Antigen
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus

HCV	Hepatitis C Virus
RNA	Riboneucleic Acid Of Hepatitis C Virus
HCC	Hepatocellular Carcinoma
HIV	Human Immune Deficiency Virus
HDL	High Density Lipo Protien
Hgb	Hemoglobin
HLA	Human Leucocyte Antigen
HPS	Hepato-Pulmonary Syndrom
HRS	Hepato-Renal Syndrom
HVAP-A	Human Vesicle Associated Membrane Protein A
HVR1	Hyper Variable Region 1
INF	Interferon
IFN α	Interferon A
IGF-1	Insulin Growth Factor-1
IgM	Immunoglobulin M
IL 28B	Interleukin 28b
INR	International Normalization Ratio
IRES	Internal Ribosomal Entry Site.
ISGs	Interferon Stimulated Genes
ITP	Immune Thrombocytopenic Purpura
IU	International Unit
KD	Kilo Dalton
LDL	Low Density Lipoproteins
LOLA	L-Ornithin, L-Aspartate

MELD	Model For End-Stage Liver Disease
MHC	Major Histocompatibility Complex
MRCP	Magnetic Resonance Cholangiopancreatography.
MRI	Magnetic Resonance Imaging
m RNA	Messenger Ribonucleic Acid
NH₄	Ammonia
NI	Nucleoside Analogue Inhibitor
NNI	Non Nucleoside Inhibitor
NS	Non Structural
PCR	Polymerase Chain Reaction
PEG-IFN	Pegylated Interferon
PFOR	Pyruvate Ferredoxin Oxireductase
PHTN	Portal Hypertension
PKR	Protein Kinase R
PLT	Platelets
Pphtn	Porto- Pulmonary Hypertension
PT	Prothrombin Time
PVT	Portal Vein Thrombosis
RVR	Rapid Virologic Response
SBP	Spontaneous Bacterial Peritonitis
SVR	Sustained Virologic Response
SR-BI	Scavenger Receptor Class B Type I
RBC	Red Blood Cell
RBV	Ribavirin

RDRP	RNA Dependent RNA Polymerase
RNA	Ribonucleic Acid
SOC	Standerd Of Care
STAT-C	Specially Targeted Antiviral Therapy For HCV
TE	Transient Elastography
TIPS	Transjugular Porto Systemic Shunt
TRIF	Toll-Like Receptor Signaling In The Liver
TSH	Thyroid Stimulating Hormone
T.bil	Total Bilirubin
Te	Transient Elastography
TGF	Tumor Growth Factor.
TMA	Transcription Mediated Amplification
U/S	Ultra Sound
USA	United States Of America
UTR	Untranslated Regions
VAMP	Vesicle Associated Membrane Protein
WBC	White Blood Cells
WHO	World Health Organization

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