A Comparative Study of the Diagnostic and Prognostic Value of Macrophage Activation Marker Soluble CD163 and Alpha Fetoprotein in Cirrhotic Patients with Hepatitis C Virus-related Hepatocellular Carcinoma treated by Loco-Regional Therapy

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بسم الله الرحمن الرحيم

وَقُلِ اعْمَلُواْ فَسَيَرَى اللّهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ

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List of Abbreviations

Abb.	Full term
5`-NPD	5`-Nucleotide phosphodiesterase
AASLD	American Association for the Study of Liver Diseases
ADAM 17-TACE	ADMN metallopeptide domain 17-tumor necrosis factor-α-converting enzyme)
AFP	Alpha-Feto Protein
AFP-L3	Lens culinarisagglutinin- reactive alpha-fetoprotein
AFU	Alpha L-Fucosidase
AJCC	American Joint Committee on Cancer
ALP	Alkaline phosphatase
ALT	Alanine Aminotransferase
ART	Anti-retroviral therapy
AST	Aspartate Aminotransferase
AUC	Area under curve
BCLC	Barcelona-Clinic Liver Cancer
BSC	Best Supportive Care
CBP	Child bearing period
CCL22	C-C motif chemokine 22
CD163	Cluster of Differentiation 163
CDC	Centers for Disease Control
CEA	Carcinoembryonic Antigen
CEUS	Contrast enhanced ultrasound
CI	Confidence Interval
CKD	Chronic Kidney Disease
CLD	Chronic liver disease
CLIP	Cancer of the Liver Italian Program

List of Abbreviations cont...

Abb.	Full term
CR	Complete response
CSF	Colony stimulating factor
CT	Computed tomography
CUPI	Chinese University Prognostic Index
DAAs	Direct Acting Antivirals
DAC	Daclatasvir
DCP	Des-gamma carboxyprothrombin
DDIs	Drug drug interactions
DM	Diabetes mellitus
DMSA	Dimercaptosuccinic acid
DNA	Deoxyribonucliec acid
DWI	Diffusion-weighted
EASL	European Association for the Study of the Liver
ECOG	Eastern Cooperative Oncology Group
EDHS	Egyptian Demographic Health Survey
eGFR	Estimated glomerular filteration rate
EHIS	Egyptian Health Issues Survey
EIA	Enzyme immunoassay
ELISA	Enzyme linked immunosorbent assay
EORTC	European Organisation for Research and Treatment of Cancer
EPO	Erythropoietin
ER	Endoplasmic Reticulum
ESCRT	Endosomal-Sorting Complex Required for Transport
ESLC	Egyptian Society of Liver Cancer
EU	European Union

List of Abbreviations cont...

Abb.	Full term
EUS	Endoscopic ultrasound
FE	Fisher Exact
GPC3	Glypican-3
HBsAg	Hepatitis B Virus surface Antigen
HBV	Hepatitis B virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C virus
HRP	Horseradish peroxidase
HSP	Heat shock protein
HTERT	Human telomerase reverse transcriptase mRNA
ICC	Intrahepatic cholangiocarcinoma
IDSA	Infectious Diseases Society of America
IFN	Interferone
IGF II	Insulin like growth factor 2
IL-8	Interleukin-8
INR	International normalized ratio
IOUS	Intraoperative ultrasound
ISDR	Interferon Sensitivity Determining Region
IU	International units
JIS	Japan Integrated Staging
JSH	Japan Society of Hepatology
KDa	Kilodalton
LA	Laser ablation
LDLT	Living Donor Liver Transplant
LED	Ledipasvir
LI-RADS	Liver imaging reporting and data system
LPS	Lipopolysaccharide

List of Abbreviations cont...

Abb.	Full term
LRT............................	Locoregional therapy
LT...............................	Liver Transplantation
MAGE........................	Melanoma antigen gene
MC.............................	Monte Carlo
MCT...........................	Microwave coagulation therapy
MELD........................	Model for End-stage liver Disease
MMP..........................	Matrix metalloproteinase
MRI............................	Magnetic resonance imaging
MSM..........................	Men who have sex with men
NAFLD......................	Nonalcoholic fatty liver disease
NASH.........................	Nonalcoholic steatohepatitis
NAT...........................	Nucleic acid testing
NHL...........................	Non Hodgkin lymphoma
NNPIs........................	Non-nucleoside polymerase inhibitors
NTRs..........................	Non-Translated Regions
OPTN.........................	Organ Procurement and Transplantation Network
ORF............................	Open Reading Frame
OS..............................	Overall survival
OST............................	Opioid substitution therapy
PAL............................	Percutaneous Acetic Acid Injection
PCR............................	Polymerase chain reaction
PDGFR	platelet-derived growth factor receptor
PEI.............................	Percutaneous Chemical Ablation
PEI.............................	Percutaneous ethanol injection
PET............................	Positron emission tomography
PMA...........................	phorbol myristate acetate

List of Abbreviations cont...

Abb.	Full term
PS............................	Performance State
PT............................	Prothrombin time
PVT..........................	Portal vein thrombosis
PWID	People who inject drugs
RBV..........................	Ribavirin
RCT..........................	Randomized control trial
RDTs........................	Rapid diagnostic tests
RFA..........................	Radiofrequency Ablation
RNA	Ribonucleic acid
ROC	Receiver operating characteristic
ROS..........................	Reactive Oxygen Species
SCCA	Serum squamous cell carcinoma antigen
sCD163	Soluble CD163
SD	Standard deviation
SHARP......................	Sorafenib Hepatocellular Carcinoma Assessment Randomized Protocol
SIM	Simeprevir
SOF...........................	Sofosbuvir
SRB 1	Scavenger Receptor B1
SRCR	Scavenger receptor cysteine-rich
STAT........................	Signal transducer and activator of transcription
SVR..........................	Sustained Virological Response
TACE	Transcatheter arterial chemoembolization
TACE-DEB..............	Chemoembolization with Drug-Eluting Beads
TAE..........................	Transarterial embolization
TAMs	Tumor-associated macrophages

List of Abbreviations cont...

Abb.	Full term
TARE	Transarterial radioembolization
TGF-beta.	Transforming Growth Factor beta
TLR	Toll-like receptor
TNF	Tumor necrosis factor
TNM	Tumor, node, and metastases
TNM	Tumor-Node-Metastasis Staging System
UCSF	University of California, San Francisco criteria
UICC	Union International Contre le Cancer.
US	Ultrasound
USA	United states of America
VEGF	Vascular endothelial growth factor
VEGFR	Vascular endothelial growth factor receptor
VIP	Vasoactive Intestinal peptide
WHO	World Health Organization

ABSTRACT

Background: hepatocellular carcinoma (HCC) shows an increasing incidence and represents the third most common cause of cancer-related death.

Aim of the Work: is to evaluate the diagnostic value of serum level of Macrophage activation marker soluble CD163 as a tumor marker for HCC and its prognostic value after transarterial chemo-embolization (TACE) or radiofrequency ablation (RFA), in comparison to alpha-feto protein (AFP).

Patients and Methods: this study was performed on 60 subjects from the outpatient Hepatology clinic and inpatient Gastroenterology and Hepatology Department at Ain Shams University Hospital. **Group I:** includes 40 randomly selected cirrhotic patients with hepatitis C virus-related hepatocellular carcinoma (excluding BCLC class D) who underwent either RFA or TACE. **Group II:** includes 20 patients with liver cirrhosis without hepatocellular carcinoma considered as control.

Results: soluble CD163 expression did not differ significantly between HCC group and liver cirrhosis group. This proves that soluble CD163 is not suitable for diagnostic use. On the other hand, soluble CD163 was associated with the severity of liver disease. Baseline soluble CD163 was significantly associated with disease progression independent of other risk factors known to be associated with an unfavorable course in HCC. Also the marked significant reduction of serum soluble CD163 levels in HCC patients subjected to either RF ablation or TACE proved that soluble CD163 may play a prognostic marker in HCC monitoring.

Conclusion: soluble CD163 is not suitable as a diagnostic marker for HCC but can be used as a prognostic marker for HCC.

Keywords: Macrophage Activation Marker Soluble CD163, Alpha Fetoprotein in Cirrhotic, Hepatitis C Virus, Hepatocellular Carcinoma, Loco-Regional Therapy