

EVALUATION OF CD49d IN B- CHRONIC LYMPHOCYTIC LEUKEMIA BY FLOW CYTOMETRY

Thesis

*Submitted for Partial Fulfillment of M.Sc. Degree
In Clinical and Chemical Pathology*

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2009

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سرطان الدم الليمفاوي المزمن (ب) باستخدام جهاز
التدفق الخلوي**

رسالة
توطئة للحصول علي درجة الماجستير
في الباثولوجيا الإكلينيكية والكيميائية

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Acknowledgement

First, I thank “**God**” for granting me the power to proceed and to accomplish this work.

I would like to express my endless gratitude and appreciation to **Prof. Dr. Salwa Saad Mostafa**, Professor of Clinical and Chemical Pathology, Ain Shams University, for giving me the honor of working under her supervision and providing me a lot of encouragement throughout this work.

I would like to express my sincere gratitude and deepest appreciation to **Prof. Dr. Manal Ahmed Shams el din El Telbany**, Professor of Clinical and Chemical Pathology, Ain Shams University, for her valuable advices, precise comments and constructive remarks throughout this work.

My deepest thanks to **Dr. Hanan Mohamed Mahmoud**, Lecturer of Clinical and Chemical Pathology, Ain Shams University, for her valuable suggestions and advices that enlightened my way in creating such a work.

Last, but not least, I would like to thank **My Dad, Mum, My Dear Husband and My Son** for their cooperation and encouragement.

INTRODUCTION

B- Cell Chronic lymphocytic leukemia (B- CLL) is a hematopoietic neoplasm of B- lymphocytes found in the peripheral blood, bone marrow, and /or lymph nodes. The morphology reveals a monomorphic small round cell population of B- lymphocytes. It is the most common adult leukemia, with a variable clinical course. Some experience an aggressive disease course that lead to premature death while others live for decades and never require therapy (***Glassman and Hayes, 2005; Shanafelt et al., 2008***).

Traditional risk parameters of CLL including Rai classification; which is a clinical staging system based on the presence of lymphadenopathy, organomegaly, and cytopenias; serum $\beta 2$ - microglobulin level and marrow infiltration patterns were the initial prognostic tools in CLL (***Kay and Shanafelt, 2007***).

Recent risk parameters were defined as prognostic markers that appear to be clearly related to the biology of B- CLL including defects detectable on fluorescence in situ hybridization, immunoglobulin heavy-chain variable region (Ig VH) mutational status, surface marker CD38, and intracytoplasmic ZAP-70 levels (***Méhes, 2005; Kay and Shanafelt, 2007***).

CD49d plays a critical role in leucocyte trafficking, activation and survival, also facilitates interactions between leucocytes and stromal cells found in the marrow or germinal center of lymphoid follicles via VCAM-1 and fibronectin. Notably, in addition to these adhesion functions, CD49d can also serve as a signaling receptor that influences B-cell survival via up regulation of Bcl-2 family members (**Shanafelt et al., 2008**).

Studies suggest that CD49d expression on CLL B-cells is lower than normal B-cells, differs from other low-grade B-cell malignancies, demonstrates intra-patient variation, and is associated with disease stage and the presence of lymphadenopathy. While several investigators have demonstrated that signaling via CD49d in CLL B cells reduces both spontaneous and drug-induced apoptosis in vitro, little is known about the prognostic importance of CD49d in patients with CLL (**Shanafelt et al., 2008**).

AIM OF WORK

The aim of this study is to evaluate CD49d expression in B-Cell Chronic lymphocytic leukemia patients and to test its impact as prognostic marker. Also, to correlate it with CD38 (prognostic marker) and markers of tumor burden as clinical staging and CD23.

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List of Abbreviations

α	Alpha
β	Beta
κ	Kappa
λ	Lambda
μ	Mu
μ L	Microlitre
ALL	Acute lymphoblastic leukaemia
AML	Acute myeloblastic leukaemia
ATM	Ataxia-telangiectasia mutated gene
Bag-1	Bcl-2 associated athanogene 1
Bax	Bcl-2-associated factor X
Bcl	B cell leukemia/lymphoma
Bcl-2	B cell leukemia/lymphoma 2
Bcl-x_L	B cell leukemia/lymphoma X long
Bcl-x_S	B cell leukemia/lymphoma X short
B-CLL	B cell chronic lymphocytic leukemia
BCR	B-cell Receptor
BM	Bone Marrow
BML	Bone Marrow lymphocyte
B-PLL	B-cell prolymphocytic leukemia
CBC	Complete blood count
CD	Cluster of differentiation
CGH	Comparative genomic hybridization
CLL	Chronic lymphocytic leukemia
CLL/PLL	Chronic lymphocytic leukemia with increased prolymphocytes
del	Deletion
dL	Decilitre
DNA	Deoxyribonucleic acid
DW	Distilled water
ECOG	Eastern co-operation oncology group

EDTA	Ethylene diamine tetraacetic acid
F	Female
FAB classification	French American British Classification
FCM	Flow cytometry
FISH	Fluorescence in situ hybridization
FITC	Fluorescein isothiocyanate
G 0	Gap 0
g	Gram
GM-CSF	Granulocyte-macrophage colony-stimulating factor
H₂O	water
Hb	Hemoglobin
HCL	Hairy cell leukemia
HLA	Histocompatibility leucocyte antigen
HM	Hepatomegaly
HMS	Hyporeactive malarial splenomegaly
HS	Highly significant
IAP	Inhibitors of apoptosis protein
Ig	Immunoglobulin
IgVH	Immunoglobulin variable region heavy gene
IL	Interleukin
IPT	Immunophenotyping
ITP	Immune thrombocytopenic purpura
IU	International unit
KD	Kilodalton
KHCO₃	Potassium bicarbonate
L	Litre
LDH	Lactate dehydrogenase
LDT	Lymphocyte doubling time
LN	Lymph node enlargement
M	Male
Mcl-1	Myeloid cell leukemia sequence 1
mL	Millilitre
MoAbs	Monoclonal antibodies

NCI-WG	USA National Cancer Institute Working Group
Na	Sodium
NaCL	Sodium chloride
NaH₂PO₄	Sodium dihydrogen phosphate
NH₄CL	Ammonium chloride
NHL	Non-Hodgkin lymphoma
NS	Non significant
p	Short arm of the chromosome
P53	(P) means protein and the number after it represents the molecular weight of this protein
PB	Peripheral blood
PBL	Peripheral blood lymphocyte
PBS	Phosphate buffer saline
PC	Personal computer
PCD	programmed cell death
PCNA	Proliferating cell nuclear antigen
PCR	Polymerase chain reaction
PE	Phycoerythrin
PH	Pleckstrin homology
PLT	Platelets
PR	Partial remission
q	Long arm of the chromosome
rpm	Revolution per minute
S	Significant
sCD23	Soluble CD23
SCT	Stem cell transplantation
SEM	Standard error of mean
SD	Standard deviation
sIg	Surface immunoglobulin
SLVL	Splenic lymphoma with villous lymphocytes
SM	Splenomegaly
SPSS	Statistical package for Social Science
TGF-β	Transforming growth factor-β
TK	Thymidine kinase

TLC	Total leukocytic count
TNF-α	Tumor necrosis factor alpha
VEGF	Vascular endothelial growth factor
VEGFR1	Vascular endothelial growth factor receptor-1
VEGFR2	Vascular endothelial growth factor receptor-2
VLA	very late antigen
VCAM-1	Vascular cell adhesion molecule-1
MADCAM-1 ..	mucosal addressin cellular adhesion molecule-1
WHO	World Health Organization
ZAP-70	Zeta- associated protein of 70 KDa

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