

Flow Cytometric Assessment of CD30 Expression in Adult Patients with Acute Leukemia

Thesis

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في المرضى البالغين المصابين CD30 تقييم التدفق الخلوي في تعبير □ بسرطان الدم الحاد

رسالة

توطئة للحصول علي درجة الماجستير في أمراض الدم الإكلينيكية

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قالوا

لسببائك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

ALCL	Anaplastic large cell lymphoma
ALL	Acute lymphoblastic leukemia
Allo HSCT	Allogenic hematopoietic stem cell transplant
AML	Acute myloid leukemia
ANOVA	analysis of variance
APL	Acute promyelocytic leukemia
APTT	Activated partial thromboplastin time
ATO	Arsenic trioxide
ATP	Adenosine triphosphate
ATRA	All trans retinoic acid
B- ALL	B- cell acute lymphoblastic leukemia
BCR-ABL1	Breakepoint cluster region –Abelson 1
BM	Bone marrow
B-NHL	B- cell non Hodgkins lymphoma
BUN	Blood urea nitrogen
CD30	Cluster differentiation 30
CD30L	Cluster differentiation 30 ligand
CD30v	Cluster differentiation 30 variant
CEBPA	CCAAT/enhancer –binding protein
CHR	Complete hematological response
c-KIT	Tyrosin kinase kit
CN-AML	Cytogenetic normal acute myloid leukemia
CNS	central nervous system
CR	Complete remession
CR1	First complete remession
CRLF2	Cytokine receptor-like factor 2
CSF	Cerebrospinal fluid
CSI	Craniospinal irradiation

List of Abbreviations

DFS	Disease free survival
DI	Direct
DLBCL NOS	Diffuse large B cell lymphoma not otherwise specifice
DS	Differentiation syndrome
DVT	Deep venous thrombosis
EDTA	Ethylenediamine tetraacetic acid
EF	Ejection fraction
EPOR	Erythropoietin receptor
ERK1	Extracellular signal –regulated kinase 1
ESR	Erythrocyte sedimentation rate
ETP	Early T-precursor
FAB	French-American-British
FDA	Food and Drug Administration
FISH	Fluorescence in situ hybridization
FLT3	Fms-like tyrosine kinase 3
GOT	Glutamate oxaloacetate transferase
GPT	Glutamate pyruvate transferase
GVHD	Graft versus host disease
H&E	Hematoxylin and eosine
HB	hemoglobin
HCT	Hemtopoietic cell transplant
HD	Hodgkins disease
HIV	Human immune deficiency viruse
HLADR	Human leukocyte antigen
HOX	Homeobox
HSCT	Hematopiotic stem cell transplant
IL-4R	Interleukin -4 receptor
INR	International normalizing ratio
IQR	Interquartile range

List of Abbreviations

ITD	Internal tandem mutation
JAK	Janus kinase
KDs	killodaltons
LDH	Lactate dehydrogenase
LFT	Liver function test
LV	Left ventricle
MAP	Mitogen activated pathway
MAPK	Mitogen-activated protein kinas
MLL	Mixed lineage leukemia
MPO	Myeloperoxidase
MRD	Minimal residual disease
MRI	Magnetic resonance imaging
N:C	nuclear to cytoplasmic
NF	Nuclear factor
NPM1	Nucleophosmin
NSE	Non spesfic esterase
OS	Overall survival
PAS	Periodic acid-Schiff
PE	Pulmonary embolism
Ph+	Philadelphia positive
PLT	Platelet
PML/RARα	Promylocytic leukemia/ retinoic acid receptor
PTD	Partial tandem duplication
qRT-PCR	Quantitative revese transcriptase –polymerase chain reaction
RA	Retinoic acid
RARs	Retinoic acid receptors
RFT	Renal function test
RTK	Receptor tyrosine kinase
RUNX1	Runt –related transcription factor 1

List of Abbreviations

RXRs	Retinoic X receptors
SBB	Sudan black B
sCD30	Serum cluster differentiation 30
SCT	Stem cell transplantation
SD	Standard deviation
SPSS	Statistical package for social sciences
T- ALL	T- cell acute lymphoblastic leukemia
T ca	Total calcium
TBI	Total body irradiation
TCR	T cell receptor
Th	T helper cell
TKI	Tyrosin kinase inhibitor
TNFRSF	Tumour necrosis factor superfamily
T-NHL	T cell non Hodgkins lymphoma
TRADD	Tumour necrosis factor receptor associated death domain
TRAF	Tumour necrosis factors associated family
WBC	White blood count
WHO	World health

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Abstract

Background: CD30, a member of (TNFR) superfamily, was originally identified as a cell-surface marker of Reed-Sternberg cell in classical Hodgkin Lymphoma, CD30 is also expressed by Several types of T- and B- cell non-Hodgkin's Lymphoma, such as anaplastic large cell lymphoma (ALCL), primary mediastinal large B- cell lymphoma (PMBCL) and Epstein-Barr-Virus (EBV)- driven clonal lymphoproliferative disorder as well as in reactive conditions such as infectious mononucleosis. **Patients and methods:** A cross-sectional study that was conducted at Clinical Hematology Department in Ain Shams University Hospital during a period from November 2016 to August 2017. 20 new cases of AML and ALL ,30 refractory / or relapsed cases of AML and ALL either T or B , enrolled in this study , CD30 % expression was assessed by flowcytometry on bone marrow sample or peripheral blood. **Results:** CD30 with cutoff >20% (+ve) was 46% of cases while cases with cutoff <20%(-ve) was 54% in all leukemia cases,CD30 expression was higher in ALL especially In T-ALL with mean value (44.564±27.158) with significant increase relapsed T-ALL (P value 0.031) followed by B-ALL (23.988±15.678). CD30 expression in relapsed AML and ALL showed an increased % but not yet statistically significant. Significant correlation was found in risk parameters as in WBCs (>100,000),PLT (<30,000) and CD30 expression in T ALL patients with P value 0.038and 0.021 respectively, and non significant between LDH and MRD in T-ALL and all risk parameters in B-ALL. ROC curve revealed that the accuracy of sensitivity and specificity was 69.9%. **Conclusion:** CD30 has been shown to be a significant diagnostic tool in cases of acute leukemia especially in newly and relapsed TALL, also it can be labeled to be targeted therapy, Drug trial using monoclonal AB to CD30 as treatment in relapsed /refractory cases with special concern to response and survival rate

Key word: MRD (minimal residual disease) tumour necrosis factor receptor(TNFR), anaplastic large cell lymphoma (ALCL), primary mediastinal large B- cell lymphoma (PMBCL) and Epstein-Barr-Virus (EBV)-
