Role of CD81 in Detection of Minimal Residual Disease in Pediatric Precursor B-Acute Lymphoblastic Leukemia

Thesis

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بسم الله الرحمن الرحيم

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صدق الله العظيم

سورة البقرة ﴿32﴾

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LIST OF ABBREVIATIONS

Abbreviation	Meaning
AA	Aplastic anemia
ABL	Abelson murine leukemia viral oncogene
AF4	Protein coding oncogene
AIDS	Acquired immune deficiency syndrome
APCs	Antigen presenting cells
ara-GTP	Arabinosyl guanine triphosphate
ATLL	Adult T-cell leukemia/lymphoma
BCDG	B cell develpmental gene(eg, PAX5, EBF1 ,LEF1, TCF3, BLNK)
BCL2	B cell lymphoma 2 gene
BCR	Breakpoint cluster region
BM	Bone marrow
c DNA	complementary deoxy ribonucleic acid
CBC	Complete blood count
CD	Cluster of differentiation
CNS	Central nervous system
CR	Clinical remission
DNA	deoxyribonucleic acid
E2A	Protein coding oncogene
EC2	Extracellular domain 2
ETV6	Protein coding oncogene
FAB	French-American-British
FC	Flowcytometry
FISH	fluorescence in situ hybridization
FITC	Fluorescein isothiocyanate
FLT3	Fms-related tyrosine kinase 3
HLA DR	Human leucocyte antigen complex DR
HTC	Hematopoietic cell transplantation
HTLV-1	Human T lymotrophic vrus
Ig	immunglobulin

LIST OF ABBREVIATIONS (CONT ...)

Abbreviation	Meaning
IGH	Immunglobulin heavy chain
Igk	Immunoglobulin light chain Kappa
IgL	Immunoglobulin light chain Lambda
Igμ	Immunoglobulin light chain μ
IHC	Immunohistochemistry
IL3	Interleukine 3
IPT	Immunophenotyping
IQR	Interquartile range
ITP	Idiopathic thrombocytopenic purpura
K2-EDTA	Di Postassium salt ethylene diamine tetra acetic acid
Kd	Kilo dalton
LEL	Large extracellular loop
MDS	Myelodysplastic syndrome
MED	Median
MFI	Mean fluorescence intensity
MLL	Mixed lineage leukemia
MoAb	Monoclonal antibody
MOLT	Human acute lymphoblastic leukemia cell line
MP	Mercaptopurines
MPOX	Myeloperoxidase
MRD	Minimal residual disease
MTX	Methotrexate
MY	Myeloid antigens
NA	Non applicable
NPV	Negative predictive Value
NS	Non significant
NSE	Non specific esterase
PAS	Periodic acid schiff
PAX5	B-cellspecific activator protien

LIST OF ABBREVIATIONS (CONT …)

Abbreviation	Meaning
PB	peripheral blood
PBX1	Pre-B-cell leukemia transcription factor 1
PC5	Phycoerythrin-Cyanine 5
PCR	Polymerase chain reation
PE	Phycoerythrin
PPV	Positive predictive value
Pre B ALL	Precursor B cell acute lymphoblastic leukemia
Pre B LBL	Precursor B cell acute lymphoblastic lymphoma
Pre T ALL	Precursor T cell acute lymphoblastic leukemia
Pre T LBL	Precursor T cell acute lymphoblastic lymphoma
RFS	Relapse free survival
ROC	Receiver operator curve
RQ PCR	Real- time quantitative polymerase chain reaction
RUNX1	Runt-related transcription factor 1
SBB	Sudan black B
STC	Stem cell transplantation
TAPA-1	Target of the antiproliferative antibody 1
TCF3	Transcription factor 3
TCR	T- cell receptors
TCR	T cell receptor
TCRD	T- cell receptor delta gene
TDT	Terminal deoxynucleotidyle transferase
TM1	Transmembrane protein 1
TM2	Transmembrane protein 2
TM3	Transmembrane protein 3
TM4	Transmembrane protein 4
TNF-α	Tumor necrosis factor α
Tspan-28	Tetraspanin 28
USA	United States of America
ZAP70	Zeta associated protein 70

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INTRODUCTION

Precursor B- acute lymphoblastic leukemia (Pre B-ALL) is a malignant disease resulting from the accumulation of genetically altered B lymphoid precursor cells. It is the most common acute leukemia in children and also can occur in adults. It is an aggressive but potentially curable disease in which monitoring the immediate and early response to therapy is of critical importance for optimal management ***(Borowitz and Chan, 2008).***

Current management protocols require assessment of residual leukemic cells at defined intervals after initiation of chemotherapy. The detection of residual leukemic cells is usually based on either molecular or immunophenotypic markers present in leukemic but not in normal cells, allowing for their specific discrimination ***(Hassanien et al., 2009).***

Flow cytometry is a powerful tool for monitoring minimal residual disease (MRD) in patients with Pre B-ALL. This approach is based on the identification of immunophenotypes expressed by leukemic cells but not by normal lympho-haematopoietic cells in bone marrow ***(Campana and Coustan-Smith, 2002).*** Flow cytometry measurement of MRD in Pre B-ALL present some particularities and difficulties to distinguish in the bone marrow neoplastic lymphoblasts of Pre B-ALL from benign B-lymphocyte precursors known as hematogones ***(McKenna et al., 2004).***

In some circumstances, the number of hematogones in the bone marrow is increased greatly, especially in children recovering from chemotherapy, aplastic conditions, other forms of bone marrow injury, and nonhematopoietic disorders. These cellular populations are especially problematic when identified in the bone marrow specimens of children after therapy for acute lymphoblastic leukemia (ALL), since