

Prognostic Significance Of Fms like Tyrosine
Kinase Receptor Internal Tandem Duplication
(FLT3-ITD) in Pediatric Acute Myeloid
Leukemia

Thesis

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To My Family With Love

List Of Contents

	Page
Acknowledgement.....	I
List of Abbreviations	II
List of Tables	IV
List of Figures.....	V
List of Photos.....	VIII
Introduction and Aim of the work	1
Review of Literature	
Chapter I: Childhood Acute Myeloid Leukemia	4
- Incidence.....	4
- Etiology	5
- Classification	5
- Pathogenesis	9
- Diagnosis	13
- Clinical manifestations of pediatric AML	13
- Laboratory features.....	15
- Treatment	34
- Prognostic factors	38
Chapter II: FLT3 Biology in Acute Myeloid Leukemia	41
- Gene mutation.....	41
- FMS like tyrosine receptor.....	42
- FLT3 Ligand	44
- FLT3 receptor signaling.....	45
- FLT3 Mutations in AML	47
- FLT3 Inhibitors	52
- Clinical implications of FLT3 ITD mutation in AML.....	53
- Other genetic mutations in AML.....	56
Chapter III: Methods of FLT3 Detection	63
- Flowcytometry	63
- Polymerase chain reaction techniques	64
- DNA sequencing	74
- DNA microarray.....	76
Subjects and Methods	78
Results	94
Discussion	113
Summary and Conclusion	127
Recommendations.....	130
References	131
Arabic summary	--

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List of Abbreviations

ALL	: Acute lymphoblastic leukemia
AML	: Acute myeloid leukemia
APL	: Acute promyelocytic leukemia
APML	: Acute promyelocytic leukemia
ATP	: Adenosine triphosphate
BAALC	: Brain and acute leukemia, cytoplasmic gene
CEBP-α	: C CAAT / enhancer binding protein-α
CR	: Complete remission
CTP	: Cytosine triphosphate
ddNTPs	: Dideoxynucleotides triphosphates
DNA	: Deoxyribonucleic acid
DSBs	: double-strand breaks
DW	: Distilled water
EMA	: Epithelial membrane antigen
FAB	: French American British
FISH	: Fluorescence in situ hybridization
FL	: FLT3 ligand
FLT3	: FMS like tyrosine kinase
GTP	: Guanosine triphosphate
HSCT	: Hematopoietic stem cell transplantation
ITD	: Internal tandem duplication
JM	: Juxta membrane
KL	: Kit ligand
MDR-1	: Multidrug resistance gene
MDS	: Myelodysplastic syndrome
MLL	: Mixed lineage leukemia gene
MRD	: Minimal residual disease

List of Abbreviations (Cont.)

NPM	: Nucleophosmin
PBS	: Phosphate buffered saline
PCR	: Polymerase chain reaction
PDGF-R	: Platelets derived growth factor receptor
PE	: Phycoerythrin
PML/RARα	: Promyelocytic leukemia gene/retinoic acid receptor α gene
PTD	: Partial tandem duplication
RNA	: Ribonucleic acid
ROS	: Reactive oxygen species
RTK	: Receptor tyrosine kinase
RT-PCR	: Reverse transcriptase polymerase chain reaction
TCR	: T-cell receptor
TTP	: Thymine triphosphate
VEGF	: Vascular endothelial growth factor
WHO	: World health organization

List Of Tables

	Page
· Table 1: FAB Classification of AML.....	6
· Table 2: WHO classification of AML.....	8
· Table 3: The association of morphology (FAB group) with cytogenetics, and immunophenotype in AML	9
· Table 4: Cytochemical stain in relation to FAB classification.....	24
· Table 5: Immunophenotypic markers in AML.....	26
· Table 6: Immunophenotyping of AML subtypes.....	27
· Table 7: Scoring of biphenotypic leukemia.....	28
· Table 8: Clinical correlations of frequent cytogenetic abnormalities observed in AML.....	30
· Table 9: Significant chromosomal abnormalities in AML.....	32
· Table 10: Potential risk factors in pediatric acute myeloid leukemia	40
· Table 11: Descriptive Clinical & laboratory data of AML patients.....	100
· Table12: Descriptive clinical & lab characteristics of AML patients with FLT3/ITD mutation	101
· Table 13: Clinical data of ITD+ve (group 1) and ITD-ve (group 2) AML patients	102
· Table 14: Laboratory data of ITD+ve (group 1) and ITD-ve (group 2) AML patients	103
· Table 15: Clinical outcome of ITD+ve (group 1) and ITD-ve (group 2) AML patients	104

List Of Figures

	Page
· Figure 1: Model of leukemogenesis with two cooperating classes of mutations	12
· Figure 2: A high power view of a bone marrow smear of M0 subtype of AML	16
· Figure 3: A high power view of a bone marrow smear of M1 Subtype of AML.....	17
· Figure 4: A high power view of a bone marrow smear of M2 Subtype of AML.....	18
· Figure 5: A high power view of a bone marrow smear of M3 subtype Of AML.....	18
· Figure 6: A high power view of a bone marrow smear shows M3v Subtype of AML.....	19
· Figure 7: A high power view of a bone marrow smear shows M4 Subtype of AML	19
· Figure 8: A high power view of a bone marrow smear shows M4Eo subtype of AML	20
· Figure 9: A high power view of a bone marrow smear shows M5a subtype of AML.....	21
· Figure 10: A high power view of a bone marrow smear showsM5b Subtype of AML.....	21
· Figure 11: A high power view of a bone marrow smear showsM6 Subtype of AML	22
· Figure 12: A high power view of a bone marrow smear showsM7 Subtype of AML	22
· Figure 13a: Non specific estrase shows positive (brown) reaction in M5.....	23
b: Myeloperoxidase stain in AML.....	23
· Figure 13-c: Combined estrase stain.	23

· Figure 13-d: Sudan black B stain positive -e: PAS stain positive in M6.....	24
· Figure 14: Potential therapeutic targets in leukemia.....	38
· Figure 15: FLT3 Receptor Structure.....	43
· Figure 16: Tyrosine kinase transferring extracellular signals to nuclear events.....	45
· Figure 17: Signal transduction pathways downstream of FMS-like tyrosine kinase-3 receptor activation	47
· Figure 18: FLT3 mutations	49
· Figure 19: Mutated tyrosine kinase signaling	51
· Figure 20: Bone marrow sections show typical morphology of myeloid blasts with cup-like nuclear invagination in AML	55
· Figure 21: Bone marrow trephine immunostained with anti-NPM monoclonal antibody shows aberrant cytoplasmic expression of nucleophosmin (NPM) in leukemic cells.....	57
· Figure 22: Schematic illustration of the Kit receptor	59
· Figure 23: Schematic drawing of a PCR cycle	65
· Figure 24: Agarose gel electrophoresis of DNA.....	66
· Figure 25: The Taqman probe	
(a)	71
(b)	71
(c)	72
· Figure 26: Mechanism of FRET probe function.....	73
· Figure 27: DNA sequencing	75
· Figure 28: Diagram shows DNA microarray.....	77

· Figure 29: Steps of conventional cytogenetic analysis	83
· Figure 30: Comparison between group 1 and 2 as regards sex.....	108
· Figure 31: Comparison between group 1 and 2 as regards clinical presentations.....	108
· Figure 32: Comparison between group 1 and 2 as regards Hb level.....	109
· Figure 33: Comparison between group 1 and 2 as regards TLC.....	109
· Figure 34: Comparison between group 1 and 2 as regards platelet count	110
· Figure 35: Comparison between group 1 and 2 as regards IPT	110
· Figure 36: Comparison between group 1 and 2 as regards cytogenetic study.....	111
· Figure 37: Comparison between group 1 and 2 as regards clinical outcome	111
· Figure 38: Kaplan Meier curve for survival time comparing group 1 and group 2 patients	112

List Of Photos

	Page
· Photo (1): A representative karyotype of an AML case (No 24) showing a normal karyotype with a modal number of (46,xy)	105
· Photo (2): A representative karyotype of an AML case (No 30) showing t(8,21) with a modal number of (46,xx).....	105
· Photo(3): Melting curve of V592A FLT3 mutation analysis	106
· Photo (4): Gel Electrophoresis for FLT3 ITD mutation shows an extra PCR band (mutant band) 370-bp in addition to the 330-bp wild band.....	107
· Photo (5): Gel Electrophoresis for FLT3 ITD mutation shows an extra PCR band (mutant band) 385-bp in addition to the 330-bp wild band	107

INTRODUCTION

Acute myeloid leukemia (AML) is a clonal malignant disease of hematopoietic tissue, which is characterized by proliferation of abnormally myeloid cells that are not mature (**Bain, 2003**).

The modern characterization of AML is a multi-disciplinary process. It requires the integration of clinical informations, morphology, cytochemistry, immuno-phenotyping, cytogenetic diagnostic techniques. It is only by bringing all these modalities together that a clear picture can be presented (**Licht and Sternberg, 2005**).

Recently, numerous recurring genetic aberrations have been identified in AML among which is FLT3 gene internal tandem duplication (FLT3/ITD). In many instances, genes altered by these aberrations have been cloned, providing insights into the mechanisms of leukemogenesis (**Bullinger and Volk, 2005**).

FLT3 is a member of the platelets derived growth factor receptor (PDGF-R) subfamily which locates at chromosome 13q12 and predominantly expressed in haematopoietic cells restricted to the CD34, positive fraction. Normal FLT3 receptor is expressed on AML blasts in most cases. While, FLT3 mutations are found in AML cases with different levels of