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

Thesis

Submitted for the Partial Fulfillment of M.D Degree
In Laboratory Haematology

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2010

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To My Family With Love

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Acknowledgement

First of all, I thank ALLAH the source of all knowledge, for blessing this work till it has reached its end as a part of his generous gifts throughout my life.

I will remain grateful to ***Prof. Dr. / Nehayet Mahmoud Azmy****, Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for her sincere supervision, kind support, help and encouragement during the progress and finalizing this work. I would like to thank her for spending much of her precious time in fulfillment of this work.*

I would like to express my deepest gratitude and appreciation to ***Prof. Dr./ Nahela Ahmed Shalaby****, Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for her kind support, advices and great help. I really feel great pleasure for working under her kind supervision.*

I am greatly indebted and grateful to ***Prof. Dr./ Sahar Samir Abd El-Mksoud****, Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for her instructive guidance, sincere supervision, encouragement, time and effort during the production of this thesis. I would like to express my deepest thanks and sincere appreciation to* ***Dr./ Dina Adel Foad****, Assistant Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for her support and encouragement. This is besides her sincere directions and her energetic help in the details of this work.*

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	**: Distelled water**
EMA	**: Epithelial membrane antigen**
FAB	**: French American British**
FISH	**: Flouresence 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	**: Phycoerythin**
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**

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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