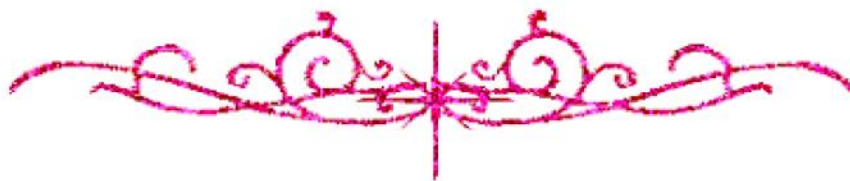


بسم الله الرحمن الرحيم





شبكة المعلومات الجامعية التوثيق الالكتروني والميكرو فيلم



جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



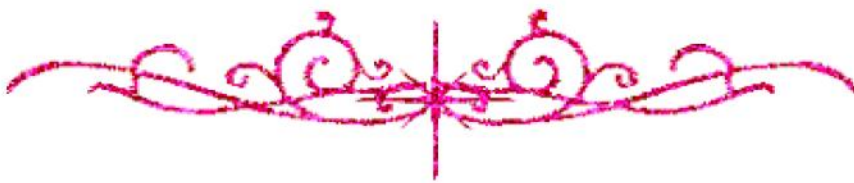
يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



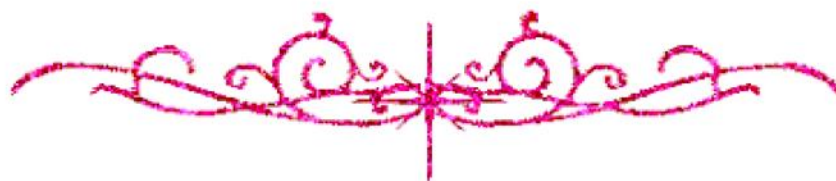


بعض الوثائق الأصلية تالفة





بالرسالة صفحات
لم ترد بالأصل





Retrospective Study about the Prevalence of (TILs) Tumor Infiltrating Lymphocytes in non-Metastatic Triple Negative Breast Cancer Patients and its Prognostic Value

Thesis

*Submitted for Partial Fulfillment of Master Degree
in Clinical Oncology and Nuclear Medicine*

By

Aya Magdy Kamal Ali

M.B.B.CH.

Faculty of Medicine – Ain Shams University

Supervised by

Prof. Dr. Hesham Ahmed ElGhazaly

Professor of Clinical Oncology and Nuclear Medicine

Faculty of Medicine – Ain Shams University

Prof. Dr. Manal Mohamed El-Mahdy

Professor of Pathology

Faculty of Medicine – Ain Shams University

Dr. Azza Mohamed Adel

Assistant Prof. of Clinical Oncology and Nuclear Medicine

Faculty of Medicine – Ain Shams University

Dr. Nermeen Mostafa

Lecturer of Clinical Oncology and Nuclear Medicine

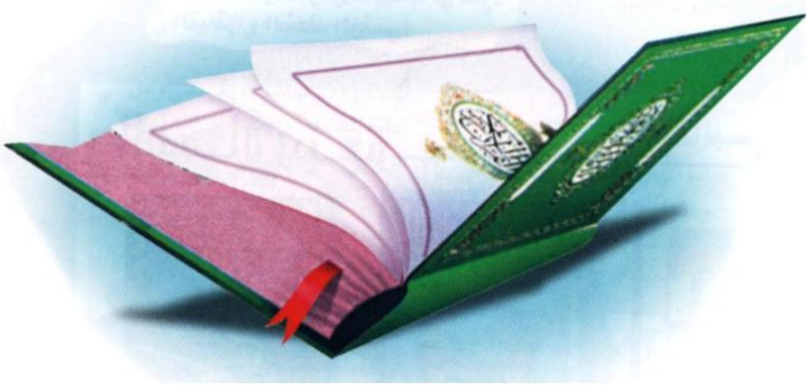
Faculty of Medicine – Ain Shams University

Faculty of Medicine – Ain Shams University

2020

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَقُلْ اَعْمَلُوا فَسَيَرَى اللَّهُ
عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ



صدق الله العظيم

[سورة: التوبة - الآية: ١٠٥]

Acknowledgments

*First and foremost, I feel always indebted to **Allah** the Most Beneficent and Merciful.*

*I wish to express my deepest thanks, gratitude and appreciation to **Prof. Dr. Hesham Ahmed ElGhazaly**, Professor of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Ain Shams University, for his meticulous supervision, kind guidance, valuable instructions and generous help.*

*Special thanks are due to **Prof. Dr. Manal Mohamed El-Mahdy**, Professor of Pathology, Faculty of Medicine, Ain Shams University, for her sincere efforts, fruitful encouragement.*

*I am deeply thankful to **Dr. Azza Mohamed Adel**, Assistant Prof. of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Ain Shams University, for her great help, outstanding support, active participation and guidance.*

*Really I can hardly find the words to express my gratitude to **Dr. Nermeen Mostafa**, Lecturer of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Ain Shams University, for her supervision, continuous help, encouragement throughout this work and tremendous effort.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Aya Magdy Kamal Ali

List of Contents

Title	Page No.
List of Abbreviations.....	5
List of Tables.....	10
List of Figures	11
Introduction	- 1 -
Aim of the Work	15
Review of Literature	
▪ Breast Cancer	16
▪ Triple-Negative BC (TNBC).....	44
▪ Tumor Infiltrating Lymphocytes in Breast Cancer	55
Patients and Methods.....	73
Results.....	78
Discussion	90
Summary.....	99
Conclusion	102
Recommendations.....	103
References	104
Arabic Summary	

List of Abbreviations

Abb.	Full term
+VE	<i>Positive</i>
ABC	<i>Advanced breast cancer</i>
ADP	<i>Adenosine di-phosphate</i>
AKT	<i>Protein kinase B</i>
AMP	<i>Adenosine mono -phosphate</i>
AR	<i>Androgen receptor</i>
ASCO	<i>American society of clinical oncology</i>
ATP	<i>Adenosine tri-phosphate</i>
BC	<i>Breast cancer</i>
BCS	<i>Breast conservative surgery</i>
BCSCS	<i>Breast cancer stem cells</i>
BCT	<i>Breast conservative therapy</i>
BHLH/LZ	<i>Basic helix loop-helix leucine zipper</i>
BL1	<i>Basal like -1</i>
BL2	<i>Basal like -2</i>
BLIA	<i>Basal -like immunoactivated</i>
BLIS	<i>Basal like immunosuppressed</i>
BMI	<i>Body mass index</i>
BRCA1	<i>Breast cancer associated gen 1</i>
BRCA2	<i>Breast cancer associated gen 2</i>
B-reg	<i>Regulatory B-cells</i>
CA15-3	<i>Cancer antigen 15-3</i>
CAP	<i>College of American pathologists</i>
CD8	<i>Cluster of differentiation -8</i>
CEA	<i>Carcino-embryonic antigen</i>
CECS	<i>Circulating endothelial cells</i>

List of Abbreviations cont...

Abb.	Full term
CIP2A	<i>Cell Proliferation Regulating Inhibitor of Protein Phosphatase 2A</i>
CK 5/6	<i>Cytokeratin 5/6</i>
CNB	<i>Core- needle biopsy</i>
CR	<i>Complete response</i>
CT	<i>Chemotherapy</i>
CTL	<i>Cytotoxic T-lymphocytes</i>
CTLA	<i>Cytotoxic T-lymphocytes associated protein</i>
D.M	<i>Diabetes Mellitus</i>
DC-1	<i>Dendritic cells-1</i>
DC-2	<i>Dendritic cells -2</i>
DCIS	<i>Ductal carcinoma insitu</i>
DFS	<i>Disease free survival</i>
DM	<i>Digital mammography</i>
DMC1	<i>Disrupted meiotic cDNA</i>
DNA	<i>Deoxyribonucleic acid</i>
DOK 7	<i>Docking protein 7</i>
EGFR	<i>Epidermal growth factor receptor</i>
EMT	<i>Epithelial mesenchymal transition</i>
EPCS	<i>Bone marrow driven endothelial precursor cells</i>
EPHA2	<i>Gen of tyrosine kinase family</i>
ER	<i>Estrogen receptor</i>
ESMO	<i>European society of medical oncology</i>
FDA	<i>Food and drug administration</i>
FGFR	<i>Fibroblast growth factor receptor</i>
FISH	<i>Fluorescence insitu hybridization</i>

List of Abbreviations cont...

Abb.	Full term
FNAC	<i>Fine needle aspiration cytology</i>
FOXP3+	<i>Fork head box P3 (FOXP3) protein</i>
GC/B-CELL	<i>Germinal center B-cell</i>
GTP	<i>Guanosine triphosphate</i>
H. T	<i>Hyper tension</i>
HATs	<i>Histone acetyl transferase</i>
HER-2	<i>Human epidermal growth factor receptor -2</i>
HLA-DR	<i>Human Leukocyte Antigen – DR isotype</i>
HRD	<i>Homologous recombination deficiency</i>
HRT	<i>Hormone replacement therapy</i>
HSP27	<i>Heat shock protein beta-1 (HSPB1)</i>
hTERT	<i>Telomerase reverse transcriptase a catalytic subunit of the enzyme telomerase</i>
IDC	<i>Infiltrating ductal carcinoma</i>
IFN	<i>Interferon</i>
IGF-IR	<i>Insulin like growth factor I receptor</i>
IHC	<i>Immunohistochemistry</i>
IL	<i>Interleukin</i>
ILC	<i>Infiltrating lobular carcinoma</i>
IM	<i>Immunomodulatory</i>
JNK	<i>Jun N-terminal kinases (JNKs) are a family of protein kinases</i>
L.N	<i>Lymph node</i>
LAR	<i>Luminal androgen receptor</i>
LCIS	<i>Lobular carcinoma insitu</i>
MAPK	<i>Mitogen activated protein kinase</i>
MBI	<i>Molecular breast imaging</i>

List of Abbreviations cont...

Abb.	Full term
MC	<i>Molecular classification</i>
MDSC	<i>Myeloid derived suppressor cells</i>
MET	<i>Hepatocyte growth factor</i>
MG	<i>Mammography</i>
MRI	<i>Magnetic resonance imaging</i>
MRM	<i>Modified radical mastectomy</i>
MSL	<i>Mesenchymal stem -like</i>
MTA1	<i>Metastasis-associated protein -1</i>
mTOR	<i>Mammalian target of rapamycin</i>
N	<i>Lymph node</i>
NCCN	<i>National Comprehensive Cancer Network</i>
NGF	<i>Nerve growth factor</i>
NK	<i>Natural killer</i>
OS	<i>Overall survival</i>
PARP	<i>Enzyme poly ADP ribose polymerase</i>
PCR	<i>Pathological complete response</i>
PD-1	<i>Programmed cell death -1</i>
PDGF	<i>Platelet-derived growth factor</i>
PDL-1	<i>Programmed cell death ligand -1</i>
PEG-10	<i>Polyethylene glycol-10</i>
PFS	<i>Progression free survival</i>
PI3K	<i>Phosphoinositide 3 kinase</i>
PR	<i>Progesterone receptor</i>
pTEN	<i>Phosphatase and tensin homolog protein</i>
RAD-51	<i>A gene which is a member of the RAD51 protein family</i>
RNA	<i>Ribonucleic acid</i>

List of Abbreviations cont...

Abb.	Full term
<i>RT</i>	<i>Radiotherapy</i>
<i>SLNB</i>	<i>Sentinel lymph nodal biopsy</i>
<i>TAA</i>	<i>Tumor associated antigen</i>
<i>TAM</i>	<i>Tumor associated macrophage</i>
<i>TGF</i>	<i>Transforming growth factor</i>
<i>TH-1</i>	<i>T- helper cell -1</i>
<i>TH-2</i>	<i>T- helper cell -2</i>
<i>TILs</i>	<i>Tumor infiltrating lymphocytes</i>
<i>TNBC</i>	<i>Triple negative breast cancer</i>
<i>TP-53</i>	<i>Gene provides instructions for making a protein called tumor protein p53</i>
<i>Tregs</i>	<i>Regulatory T-cells</i>
<i>TSLP</i>	<i>Thymic stromal lymphopoietin</i>
<i>VEGF</i>	<i>Vascular endothelial growth factor</i>
<i>Vs</i>	<i>Versus</i>
<i>X</i>	<i>Capecitabine</i>

List of Tables

Table No.	Title	Page No.
Table (1):	Genomic TNBC subtypes and potential therapeutic targets.....	50
Table (2):	Systemic Treatment For Tnbc	52
Table (3):	Patient descriptive data:.....	80
Table (4):	Tumor characteristics and received treatment:.....	81
Table (5):	Relationship between CD8+ and clinic-pathological characteristics:	82
Table (6):	Relationship between CD8+ and clinic-pathological characteristics:	83
Table (7):	Percentages of CD8 as a marker to TILs:	84
Table (8):	Disease-free survival duration in months for all patients:	86
Table (9):	Correlation between CD8+TILS percentage & progression-free survival duration:	87
Table (10):	Overall survival duration in months for all patients:	88
Table (11):	Correlation between CD8+TILS percentage & overall survival duration:.....	89