Node Negative Breast Cancer In Egyptian Patients At The National Cancer Institute, Cairo University: Correlation With Tumor Size and Molecular Classification.

Protocol of Thesis

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BY

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Abstract

Background: Node-negative breast cancer is a prevalent form of the disease worldwide, particularly in regions with rigorous screening and disease awareness efforts. Although there is a common biology between node negative and node positive breast tumors, it is still important to specifically address risk assessment and predictive factors in node negative breast cancer **(Harbeck and Thomssen, 2011).** Different breast cancer subtypes were newly recognized based on immunohistochemistry for ER, PR, HER2/neu and Ki-67, reflecting on patients' prognosis and management. We conducted this study to determine the prevalence of breast cancer subtypes in Egypt (National Cancer Institute, Cairo University) according to immunohistochemistry panel and to explore their association with node negative and other prognostic factors.

Material and Methods: A retrospective study carried out on one hundred and thirteen cases diagnosed as node negative invasive breast carcinoma at the Pathology Department, National Cancer Institute (NCI), Cairo University during the period from January 2007 to December 2010. The cases were classified into luminal A, luminal B, luminal-HER2/neu, HER2/neu-enriched and TNBC, using immunohistochemistry (ER, PR, HER2/neu and Ki-67). The obtained results were correlated with clinico-pathologic variables as well as 5-year DFS and 5-year OS.

Results: Cases were categorized into luminal A (31%), luminal B (35.4%), luminal HER2/neu (9.7%), HER2/neu-enriched (12.4%) and TNBC (11.5%). The majority of cases (85.8%) were low grade while the remaining

cases (14.2%) were high grade. The difference was statistically significant (P value 0.001). Her2-negative cases showed slightly better 5-year DFS than Her2-positive cases with borderline statistical significant difference (89.3% versus 81.7%; respectively) (p=0.131). DFS estimates were not significantly different (*P* 0.975) among different breast subtypes with worst 5-years DFS for TNBC subtype (81.5%). OS estimates were near significantly different (*P* 0.145) among different breast subtypes whereas TNBC subtype had the worst 5-year OS (49.5%).

Conclusions: TNBC subtype is considered the worst breast cancer subtype. Luminal B is intermediate subtype with variable outcome. Luminal A, luminal HER2/neu and HER2/neu-enriched are expected to behave favorably. OS is expected to be better among hormone-positive versus hormone negative cases. Regarding to HER2 status, HER-2-negative cases achieved better 5-year OS than HER2-positive cases.

By the end of the current study, the conclusion that was achieved is that there wasn’t substantial difference in the underlying tumor biology between node-negative and node-positive disease, and the node-negative breast cancer didn’t automatically suggest a good prognosis or requiring chemotherapy, and additional biomarkers are needed to help identify those node-negative patients who are expected to behave favorably.

LIST OF CONTENTS

LIST OF Figures

Page

LIST OF TABLES

Page

LIST OF ABBREVIATIONS

- **ADH:** Atypical ductal hyperplasia
- **AgNOR:** Argyrophilic nucleolar organizer regions
- **AJCC:** American Joint Committee on Cancer
- **ALH:** Atypical lobular hyperplasia
- **ASCO:** American Society of Clinical Oncology
- **ATM:** Ataxia telangiectasia mutated
- **BC:** breast cancer
- **BCS:** breast conservative surgery
- **BM:** bone marrow.
- **BMI:** body mass index
- **BrdU:** Thymidine labeling index, bromodeoxyuridine
- **CDK:** cyclin-dependent kinase
- **CISH:** Chromogenic in situ hybridization
- **DAB:** 3, 3’ diaminobenzinetetrachloride
- **DCIS:** Ductal carcinoma in situ
- **DHEA:** Dehydroepiandrosterone
- **DIN:** Ductal intraepithelial neoplasia
- **DFS:** Disease free survival

- **EGFR:** epidermal growth factor receptor
- **ELISA:** enzyme-linked immunosorbent assay
- **ER:** Estrogen receptor
- **ERK:** Extracellular-signal regulated kinase
- **ETD:** extralobular terminal duct
- **FISH:** Fluorescence in situ hybridization
- **HER2:** The human epidermal growth factor receptor 2 gene
- **HER/ErbB:** human epidermal growth factor
- **HT:** Hormonal therapy
- **H & E:** hematoxilin and eosin staining
- **IARC:** International Agency for Research and Cancer
- **IDC:** invasive ductal carcinoma
- **IHC:** immunohistochemistry
- **IM:** internal mammary node
- **ITD:** intralobular terminal duct
- **(i+):** +ve by IHC
- **Ki-67 LI:** Ki-67 labeling index
- **LBD:** ligand binding domain
- **LCIS:** Lobular carcinoma in situ
- **LIN:** Lobular intraepithelial neoplasia

- **LFS:** Li-Fraumeni syndrome
- **LN:** lymph node
- **LR:** local recurrence
- **M:** distant metastases
- **MAP kinase:** mitogen activated protein kinase
- **MoAbs:** Monoclonal antibodies
- **MRI:** Magnetic resonance imaging
- **N**: regional lymph nodes
- **NBF:** Neutral buffered formalin
- **NCCN:** National Comprehensive Cancer Network
- **NCI:** National Cancer Institute
- **NGS:** Nottingham Grading System
- **NOS:** not otherwise specified
- **NST:** no special type
- **PAI-1:** plasminogen activator inhibitor-1
- **PARP inhibitors:** Poly(ADP-Ribose)polymerase inhibitors
- **PCB's:** polychlorinated biphenyls
- **PCR:** polymerase chain reaction
- **pCR:** pathologic complete response
- **PJS:** Peutz-Jeghers syndrome

- **PKB :** Protein Kinase B
- **PR:** Progesterone receptor
- **PTEN:** phosphatase and tensin homolog
- **RT-PCR:** reverse transcriptase polymerization chain reaction
- **RR**: regional relapse
- **SEER**: Surveillance, Epidemiology, and End Results
- **SISH:** Silver-enhanced in situ hybridization
- **T:** primary tumor
- **TDLU:** Terminal duct-lobular unit
- **TGFβ:** transforming growth factor beta
- **Tis:** Carcinoma in situ
- **Tis (DCIS):** Ductal carcinoma in situ.
- **Tis (LCIS):** Lobular carcinoma in situ.
- **TNBC:** triple-negative breast cancer
- **Tis (Paget's):** Paget's disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma.
- **UICC:** International Union for Cancer Control
- **Upa:** urokinase plasminogen activator
- **WHI:** Women's Health Initiative