Tamoxifen with or without Ovarian Function Suppression as Adjuvant Hormonal Treatment in Premenopausal Breast Cancer Patients

Thesis

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List of Abbreviations

Abb.	Full term
ABCSG-12	*The Austrian Breast and Colorectal Cancer Study Group phase III Trial*
AIs	*Aromatase inhibitors*
ASCO	*American Society of Clinical Oncology*
BCDDP	*Breast Cancer Detection Demonstration Project*
BCRAT	*Breast Cancer Risk Assessment Tool*
BCS	*Breast conservative surgery*
BMD	*Bone mineral density*
BMI	*Body mass index*
BRCA	*Breast cancer gene*
CCNE1	*Cyclin E1*
CI	*Confidence interval*
CNB	*Core needle biopsy*
CR	*Complete response*
CT	*Computed tomography*
CTCAE	*Common Terminology Criteria for Adverse Events*
DCIS	*Ductal carcinoma in situ*
DFS	*Disease free survival*
DNA	*Deoxy-nucleic acid*
E-3193	*Eastern Cooperative Oncology Group trial 3193*
EBCTCG	*Early Breast Cancer Trialists' Collaborative Group*
ECOG	*Eastern Cooperative Oncology Group*
EDBC	*Endocrine-dependent breast cancer*
EGFR	*Epidermal growth factor receptor*

List of Abbreviations (Cont...)

Abb.	Full term
ER	*Estrogen receptor*
ERE	*Estrogen response elements*
ET	*Endocrine therapy*
FDA	*U.S. Food and Drug Administration*
FDG	*Fluorodeoxyglucose*
FGF	*Fibroblast growth factor*
FNA	*Fine needle aspiration*
FSH	*Follicle-stimulating hormone*
GGH	*Gamma glutamyl hydrolase*
GK	*Gamma knife*
GnRH	*Gonadotropin-releasing hormone*
HDL	*High -density lipoprotein*
HER	*Human epidermal receptor*
HER2	*Human epidermal growth factor-2 receptor*
HR	*Hormonal receptor*
LAPTMB4	*Lysosome-associated transmembrane protein 4-beta*
LBD	*Ligand-binding domain*
LCIS	*Lobular carcinoma in situ*
LDL	*Low-density lipoprotein*
LH	*Luteinizing hormone*
LHRH	*Luteinizing hormone-releasing hormone*
LVI	*Lymphovascular invasion*
M	*Metastatic disease*
MAPK	*Mitogen activated protein kinases*
MDR-1	*Multidrug-resistant gene 1*
MIBB	*Minimally-invasive breast biopsy*
N	*Lymph node*
NCCN	*National Comprehensive Cancer Network*

List of Abbreviations (Cont...)

Abb.	Full term
NSABP	*National Surgical Adjuvant Breast and Bowel Project*
NSEP1	*Nuclease sensitive element binding protein 1*
OS	*Overall survival*
PFS	*Progression free survival*
PR	*Progesterone receptor*
ROLL	*Radio guided occult lesion localization*
RS	*Recurrence score*
RTK	*ReceptorTyrosine Kinase*
SDF- 1	*Stromal cell-derived factor*
SEER	*Surveillance, Epidemiology, and End-Results*
SERDs	*Selective estrogen receptor down-regulators*
SERMs	*Selective oestrogen receptor modulators*
SLNB	*Sentinal lymph node*
SOFT	*Suppression of Ovarian Function Trial*
SRC-1	*Steroid receptor coactivator-1*
T	*Tumor size*
TEXT	*Tamoxifen and Exemestane Trial.*
TNBC	*Triple negative breast cancer.*
VEGF	*Amphiregulin and Vascular endothelial growth factor*
WGL	*Wire-guided localization*

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer globally and is the leading cause of cancer-related death in women. The American Cancer Society estimates that 249, 260 Americans will be diagnosed with invasive breast cancer and 40, 890 will die of the disease in the United States in 2016 ***(Siegel et al., 2016).***

The treatment of breast cancer includes the treatment of local disease with surgery, radiation therapy, or both, and systemic treatment with chemotherapy, endocrine therapy, biologic therapy, or combinations of these. The need for and selection of various local or systemic therapies are based on several prognostic and predictive factors. These factors include tumor histology, clinical and pathologic characteristics of the primary tumor, ALN status, tumor hormone receptor (ERlPR) content, tumor HER2 status *(**NCCN Guidelines Version 2.2016**)*.

Adjuvant endocrine therapy is an integral component of care for endocrine-dependent breast cancer (EDBC). The goal of this type of therapy is to counteract the production and the action of estrogens ***(Jankowitz et al., 2013)***.

Adjuvant endocrine therapy with tamoxifen had been recommended for premenopausal women with hormone

receptor positive breast cancer during the past 15 years ***(Howlader et al., 2013)***.

The American Society of Clinical Oncology endorsed guidelines recommending that ovarian ablation or suppression not be added routinely to adjuvant therapy in premenopausal women ***(Griggs et al., 2012).***

International consensus guidelines for breast cancer management in young women suggested that the addition of a gonadotropin-releasing hormone (GnRH) agonist to tamoxifen be discussed on an individualized basis ***(Partridge et al., 2014).***

AIM OF THE WORK

This is a retrospective study aiming at evaluating the disease free survival, overall survival &toxicity profile in premenopausal breast cancer patient receiving *Tamoxifen* versus Tamoxifen with ovarian suppression (LHRH) agonists as adjuvant hormonal treatment

Chapter 1
EPIDEMIOLOGY AND RISK FACTORS OF BREAST CANCER

1- Epidemiology

In the United States, breast cancers remains the most frequent cancer in women and the second most frequent cause of cancer death. In 2017, it is estimated that approximately 252, 710 women will be diagnosed with invasive breast cancer, and 41, 610 women will die from the disease. Breast cancer death is expected to down by 34% as a result of improvements in early detection and treatment ***(Jemal et al., 2017)***.

Breast cancer is the most common cancer among women in Egypt. The proportion of breast cancer among Egyptian females was 32.0% followed by liver cancer 13.5%. The age standardized rate and the crude incidence rate for breast cancer per 100, 000 in lower Egypt (2009 to 2011) were 53 and 43.8, in middle Egypt (2009) were 35.6 and 25.8 and in upper Egypt (2008) were 64.5 and 45.3 respectively ***(Amal et al., 2014).***

The total number of breast carcinomas in Ain Shams University was 2808 cases representing 99.5% of all malignant breast tumors and 23.9% of the total malignancies ***(Thanaa et al., 2015).***

Breast cancer is the most common cancer among females (2002-2010), accounting 37.5% in National Cancer Institute and 19.6% in both genders ***(Nelly et al., 2014)***

In the early 1980s, breast cancer rates rose steeply by 3.7 percent per year over the baseline incidence. After increasing from 1994 to 1999, breast cancer incidence rates remained stable from 2000 to 2009. The increase in breast cancer incidence through the 1990s was seen mostly in early stage and in situ cancers, and was attributed to increased detection of early stage disease because of screening. However, environmental factors and increased lifetime estrogen exposure likely also contributed to the higher incidence ***(Jemal et al., 2013).***

2- Risk factors

Multiple factors were associated with an increased risk of developing breast cancer, but the majority of these factors convey a small to moderate increase in risk for any individual woman ***(Jemal et al., 2009).***

- ***Age:***

It has been estimated that approximately 50% of women who develop breast cancer have no identifiable risk factor beyond increasing age and female gender. The importance of age as a breast cancer risk factor is sometimes overlooked. In 2009, it was estimated that 18, 640 invasive breast cancers and