شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

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قسم

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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

HANAA ALY

A Retrospective Analysis of Clinicopathological Data and outcomes of Hormonal Positive Her2 Negative Metastatic Breast Cancer Patients in Clinical Oncology Department in Ain Shams University Hospitals in Egypt, Ain Shams Clinical Oncology Registry (ASCOR)

Thesis

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✍ *Sylvia Amgad Ragheb Kozman*

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List of Abbreviations

Abbr.	Full-term
CDK	**:** Cyclin-dependent kinase
CI	**:** Confidence interval
DFS	**:** Disease-free survival
DM	**:** Diabetes Miletus
DNA	**:** Deoxyribonucleic acid
ECOG	**:** Eastern Cooperative Oncology Group
ER	**:** Estrogen receptor
ET	**:** Endocrine therapy
FACT	**:** Fulvestrant and Anastrozole Combination Trial
FDA	**:** Food and drug administration
FISH	**:** Fluorescence In-situ-hybridization
HCV	**:** Hepatitis C virus
HER2	**:** Human epidermal growth factor receptor 2
HR	**:** Hazard ratio
HTN	**:** Hypertension
IHC	**:** Immunohistochemistry
IHD	**:** Ischemic heart disease
MBC	**:** Metastatic breast cancer
NSAI	**:** Non-steroidal aromatase inhibitor
ORR	**:** Objective response rate
OS	**:** Overall survival

PFS	**:** Progression-free survival
PgR	**:** Progesterone receptor
PIK3CA	**:** Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha
PS	**:** Performance status
QoL	**:** Quality of life
SD	**:** Standard deviation
SERM	**:** Selective estrogen receptor modulator
SPSS	**:** Statistical package for social science
SWOG	**:** Southwest Oncology Group
UK	**:** United Kingdom
USA	**:** United States of America

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Abstract

Background: Breast cancer is the most prevalent cancer in women in the world. Estrogen receptor modulators and estrogen deprivation have become standards of care for hormonal positive Her2 negative metastatic breast cancer patients. However, after traditional first-line endocrine monotherapy treatment, the disease typically progresses despite the initial high rate of clinical benefit. Multiple studies have aimed at optimizing treatment strategies to improve clinical benefit beyond the traditional single-agent endocrine treatment.

Aim of the Work: To analyse retrospectively clinic-pathological outcome of hormonal positive Her2 negative metastatic breast cancer patients treated in clinical oncology department in Ain Shams University hospitals in Egypt during the period from January 2017 till December 2019.

Patients and Methods: This is a retrospective study which included 104 hormonal positive Her-2 negative metastatic breast cancer female patients attending the breast clinic at the Clinical Oncology Department, Ain Shams University during the period between January 2017 till December 2019.

Result: Overall, of the 104 patients in the present study, eleven patients lost follow up, forty-two patients (40.4 %) died, and fifty-one patients (49 %) are alive till the end of our follow up. The median OS is 45.47 months, while the median PFS is 10.98 months. Age had a significant impact on PFS where patients aged more than 50 years had longer PFS (13.95 months) than those patients younger than 50 years (9.3 months) (P=0.034). Patients with metastatic breast cancer from the start were associated with longer progression free survival (PFS) (13.9 months), in comparison to patients metastatic after neoadjuvant chemotherapy (6.9 months) and after adjuvant chemotherapy (9.3 months),

In the present study, regarding previous adjuvant hormonal treatment in recurrent breast cancer patients, those who received tamoxifen as prior adjuvant hormonal treatment had median OS 59.28 months and PFS 13.94 months, however, patients who did not receive tamoxifen as adjuvant hormonal treatment had median OS 37.68 months and PFS 7.86 months. Patients who received Aromatase inhibitors as prior adjuvant hormonal treatment had median PFS 13.94 months however, patients who did not receive AI as adjuvant hormonal treatment had median PFS 9.6 months.

Conclusion: In general, endocrine therapy represents the mainstay for most patients with hormone receptor positive metastatic breast cancer patients. Many prognostic factors impact survival in patients with hormone receptor positive Her2 negative advanced breast cancer.

Key Words: metastatic, breast cancer, endocrine therapy, prognostic factor, progression free survival, overall survival.

Introduction

Breast cancer is the most common malignancy among women in the world and the leading cause of cancer death among females **(Sung et al., 2021).** Despite the advances in the diagnosis and the treatment of breast cancer, 6–10% of affected patients present metastatic breast cancer at diagnosis, and 30–40% will develop metastasis during the evolution of their disease **(Dawood et al., 2010)**, **(Fodor et al., 2011).**

About two-thirds of breast cancers are hormone receptor-positive **(Tsiftsis, 2014).** Hormone receptor-positive cancers tend to grow more slowly and are more likely to respond to hormonal therapy.

The treatment of metastatic breast cancer has evolved rapidly in the last 20 years **(Torre et al., 2015)**, As 60–70% of metastatic breast cancer patients are hormonal receptor-positive **(Hewison & Kuras, 2005),** the mainstay treatment is endocrine therapy (ET), this form of treatment targets the production of estrogen in the body or blocks the function of estrogen in the cancer cell directly**(Kelly et al., 2017)**. The hormonal therapy includes tamoxifen a selective estrogen receptor modulator (SERM) that binds competitively to estrogen receptors and can have both antagonistic and agonistic effects depending on the tissue action.

The use of aromatase inhibitors can be used in post-menopausal women, Aromatase inhibitors include nonsteroidal aromatase inhibitors (anastrozole and letrozole) and steroidal aromatase inhibitors (exemestane). Aromatase inhibitors block the action of peripheral aromatase, preventing the conversion of androgen to estrogen. **(Bonneterre, 2012).**

The third class of endocrine therapy is fulvestrant, a selective estrogen receptor degrader **(Leo et al., 2014).**

Traditional endocrine therapy at the frontline setting achieves an overall response rate in the range of 25–45% and median PFS around 8–10 months **(Mouridsen et al., 2003)** Although ET is typically able to delay disease progression, almost invariably, patients will experience a relapse of their disease. As disease progression is thought to represent the development of systemic resistance to ET, typically disease progression prompts a change in therapy often to a second-line ET **(Kelly et al., 2017).**

Unfortunately, with time, the disease progression will continue to occur, necessitating further changes in therapy often through multiple lines of endocrine therapy, targeted therapy, and cytotoxic therapy.

Over the last decade, thanks to a combination of new therapeutic agents and diagnostic strategies, the outcome, and

management of patients with metastatic breast cancer gradually improved both from survival and quality of life standpoint.

Development of new agents such as CDK4/6 inhibitors, mTOR inhibitors, and PIK3CA inhibitors have prolonged survival time after recurrence for patients with hormone receptor-positive Her2 negative metastatic breast cancer **(Hattori et al., 2021)**.

The combination of CDK4/6 inhibitors (CDK4/6I) with endocrine therapy has significantly increased progression-free survival (PFS) of first- and second-line treatments in patients with hormone receptor-positive, HER2 negative (luminal) metastatic breast cancer **(Basile et al., 2021)**

Therefore, it is important to plan the treatment strategy for hormone receptor-positive, Her2 negative (luminal) metastatic breast cancer. considering the remaining life expectancy.