Outcome of Anthracycline versus Taxane Based Regimens on Different Metastatic Sites in Breast Cancer

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Abstract:

Background: Breast cancer holds a wide spectrum of heterogeneity in terms of gene expression, immunophenotypes, treatment response and clinical outcomes. Metastatic breast cancer is an incurable disease and the main aims of treatment are survival prolongation and improvement quality of life. Median survival is established by tumor biology, therapy response, patient tolerance to treatment and comorbid diseases. The overall median survival for each subgroup is approximately 2.5 years. Several studies suggested that the regimens based on anthracycline are better than regimens based on taxanes in the progression time. Our study aims to evaluate comparison between anthracycline versus taxanes containing regimens in treatment of metastatic breast cancer patients.

Material and Method: This is a retrospective cohort study of 225 cases of metastatic breast cancer at Medical Oncology Department of South Egypt Cancer Institute, Assiut University in the timeline between January 2013 to December 2018. Patients were selected to be pathologically confirmed metastatic disease at time of presentation or recurrence after surgery with different pathological subtypes in female patients to assess comparison between anthracycline versus taxanes containing regimen in treatment of metastatic breast cancer patients and their effect on different metastatic sites and on survival.

Result: Clinicopathological criteria was almost balanced between the two groups including age, menopausal status, tumor size, nodal status, distant metastasis, tumor grade, histo-pathological criteria, hormonal status and site of metastasis. The patients with liver metastases shown more significant response with anthracycline based regimen than with taxane based regimen (80.0% vs 35.7% P value <0.001) but the response rate of other metastatic sites in both groups were nearly comparable. The patients who received taxane based regimen shown higher OS than the patients who received anthracycline based regimen (74.5 ± 5.2% vs 54.9 ± 6.5% P value 0.015) but no difference appeared in PFS on both groups.

Conclusion: Anthracycline based regimen shows significant improvement in response rate in patients with liver metastases in comparison to taxane based regimen while the patients who received taxane based regimen show more significant OS but no difference in PFS in both groups.

Keyword: metastatic breast cancer, anthracycline, taxanes, metastatic sites, RR, PFS, OS.

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Introduction:

Breast cancer is one of the leading causes of death globally. Female breast cancer has exceeded lung cancer as the leading cause of global cancer incidence in 2020, with an estimated 2.3 million new cases, representing 11.7% of all cancer cases [1]. In Egypt, breast cancer (BC) is the second-leading cause of mortality among women, it accounts for 33% of female cancer cases and more than 22,000 new cases diagnosed every year. Cancer incidence rate in general is 157.0 per 100,000 female Egyptian with the highest rate to BC, by the year 2050, cancer rates are expected to increase to be three-fold [2].

Metastatic breast cancer may occur in a variety of clinical scenarios, ranging from solitary metastatic lesions to diffuse and multiple organ involvement [3].

The disease stage, histo-pathological grade and expression of the tumor receptors for estrogen, progesterone and human epidermal growth factor are the cornerstones of current prognostic and predictive algorithms [4].

Dissemination of cancer cells has predominantly been reported to the bones, lungs, liver, brain, in addition to lymph nodes [5]. With the bone is the most while the brain is the least-affected metastatic sites [6]. Unusually, the absence of lung relapse was reported in the luminal A subtype, while brain metastasis was mostly found in patients with basal like breast cancer (BLBC) and HER2+ breast cancer [7]. The incidence of lung metastasis can increase up to 40% in triple negative breast cancer (TNBC) compared with only 20% in non-TNBC. Gene expression analysis reported that lung relapse patients were more detected in the luminal B and basal subtypes, whereas bone relapse was less frequent in basal like breast cancer (BLBC) [8].

Metastatic breast cancer is an incurable disease and the main therapy goals are survival prolongation and enhancement of quality of life [9]. Overall median survival is nearly 2.5 years and is determined by tumor biology, therapy response, and patient tolerance of therapy in addition to comorbid illnesses [10].

Many previous studies stated that the involvement of visceral metastases, especially liver metastases is a sign of poor survival as the median survival time in the patients with breast cancer and liver metastases is only 4–8 months without treatment [11]. Meanwhile the patients survival with lung metastasis has the best clinical outcome in hormonal positive breast cancer patients, however HER2+ patients subtypes and TNBC have the worst prognosis [12]. For patients with metastases only to the lung, the prognosis is exceptionally poor with a median survival of 25 months only [13].

Treatment of MBC differs according to many factors like toxicity risk, the patient preferences, the tumor burden, the tumor characterization itself such as HER2 status and hormone receptor status, age, history of prior therapy, co-morbidities, degree of tumor-related symptoms, and metastasis sites [14].

For systemic therapy options, many therapeutic chemotherapy agents like capecitabine, cyclophosphamide, 5-fluorouracil, methotrexate, vincristine, cisplatin, etoposide, vinorelbine and gemcitabine are shown effectiveness in the treatment of brain metastases, with an objective response rate about 30%, and a median OS of up to 31 weeks [15].

Anthracyclines signify as the most common anti-tumor antibiotics used in the management of MBC. About 30–40% of MBC patients with anthracycline therapy reported survival response within 22 months [16]. The regimens based on anthracycline are better than the regimens without anthracycline in the term of the progression time; however, they are associated with greater toxicity with no improvement in OS [17].

Taxanes are microtubule inhibitors that decrease tumor angiogenesis and are considered as the first-line treatment in the patients who show resistance to anthracycline or cannot receive additional anthracycline treatment [18] and show higher response rate in anthracycline-resistant MBC patients with survival response about 63.6 months [19].

No global agreement exists regarding the ideal treatment strategy for MBC and no guidelines are available [20]. Although many randomized trials of some first-line regimens have reported better survival and quality of life (QoL) as well as few studies have mentioned the effectiveness of chemotherapy beyond first-line agents. Excluding hormonal therapy, anthracycline- and taxane-based regimens are considered the first-line chemotherapy agents for human epidermal growth factor 2 (HER2) negative MBC [21].

This research discussed the comparison between the two groups of metastatic breast cancer patients who received anthracycline based regimen versus taxane based regimen and their impact on response rate and survival outcomes (PFS, OS) on different metastatic sites.

Materials and Methods:

Study design and patients' methods

A retrospective cohort study of 225 cases metastatic breast cancer at Medical Oncology Department of South Egypt Cancer Institute, Assiut University in the timeline between January 2013 to December 2018 with follow up till August 2022. Pathological diagnosis was revised and confirmed by the pathologist in cases of female patients, age ≥ 18 years, who had qualified and sufficient medical record. All medical records of the patients were assessed for clinico-pathological data including age, site, size, tumor invasion, lymph node metastasis, lympho-vascular invasion, perineural invasion and distant metastases.

Patient stratification:

We arranged the analyzed patients according to the patient-interrelated factors including the age group (less than 50 years vs. 50 years or more), the Eastern Cooperative Oncology Group (ECOG) performance status (grade 0/1 vs. grade 2), and the menopausal status (pre/perimenopausal vs. postmenopausal); as well as the tumor-related factors like the histo-pathological subtypes (ductal vs. lobular vs. other types), the pathological grade (I/II vs. III) based on the Nottingham grading system [22], the type of metastatic disease (de novo vs. recurrent) and the number of metastasized organ/s (solitary vs. multiple) and with comparison made between the anthracycline vs taxanes based regimens (their response rate, PFS, OS).

Treatment and tool of assessment:

Anthracycline and taxane based regimens were given according to the local protocol and treatment was continued until maximal response, unacceptable toxicity, or patient’s refusal to continue. Dose modifications were done according to the local protocol. The response rate was constructed upon the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) [23].

Statistical methods:

All statistical calculations were performed using SPSS (statistical package for the social science; SPSS Inc., Chicago, IL, USA) version 22. Quantitative data were statistically detailed in terms of mean ± SD and median (range) according to status of normal distribution. Qualitative data were statistically detailed in terms of frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparison of quantitative variables was done using student t test. For comparing the categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Kaplan-Meier's method with log rank test was operated for calculation of progression free and overall survival analysis. P-value was set significant at 0.05 level. The Response Evaluation Criteria in Solid Tumors, version 1.1, was used to calculate the efficacy for measurable or evaluable lesions using the clinical or radiologic findings. PFS of the patients receiving each drug termed as the interval from the date of the first administration of the specific drugs to the date of the first stated tumor progression or death from any cause. OS of the patients termed as the interval from the diagnosis of distant metastases (DM) to death from any cause or the last available follow-up date. DFI termed as the interval between surgery and the date of diagnosis of the first distant relapse. ORR termed as sum of rates of complete response (CR) and regressive disease (RD). Clinical data, such as patients' performance status, age and the presence of visceral involvement were gathered at the initiation of the first-line chemotherapy for MBC patients. In addition, the data on HR and HER2 status, as well as types of adjuvant systemic treatment were collected for all patients from their medical records. Patients with an initial diagnosis of metastatic disease were defined as synchronous MBC, others who developed DM after receiving adjuvant treatment were defined as metachronous MBC. In the present study, we defined HR positive disease as > 10% of tumor cells with ER or PR expression on immunohistochemical analysis. OMBC was defined as MBC with single or few detectable metastases less than or equal to three in one site.

Results:

Clinic-pathologic characteristic of the patients:

The patients who received anthracycline based regimen about fifty-four (48.6%) patients presented with advanced T, while the patients who received taxane based regimen about sixty-eight (59.6%) patients with early T stage, and sixty-four (56.1% P value 0.001) patients underwent curative breast surgery. Other factors are comparable.

The MBC patients who presented with liver, lung, bone and local metastasis were more received anthracycline based regimen in comparison with receiving taxane based regimen which was about (27.9% vs 16.7% P value 0.043), (36.0% vs 22.8% P value 0.029), (34.2% vs 20.2% P value 0.018) and (65.8% vs 40.4% P value <0.001) respectively. Full baseline data is shown in Table 1.

Majority of the patients who received taxane based regimen were presented with luminal B molecular subtype in comparison to the patients who received anthracycline based chemotherapy (51.9% vs 38.7% P value <0.001) respectively as shown in Table 2. Site of metastasis on the studied metastatic BC patients are shown in Table 3.

Comparison of response rate between anthracycline-based and taxane- based chemotherapy on the studied MBC patients:

According to the order of the palliative treatment, most of the patients were received anthracycline based regimen as a first line therapy in comparison with the patients who were received taxane based regimen while as a second line therapy the patients who received taxane based regimen were with higher incidence than the patients who patients received anthracycline based regimen (74.8 % vs 44.7%, 40.4% vs 12.6% P value <0.001) respectively.

According to the response rate, the patients with liver mets were shown more significant RR with receiving anthracycline based regimen as a palliative line therapy than with receiving taxane based regimen (80.0% vs 35.7% P value <0.001) respectively. These findings are shown in Figure 1.

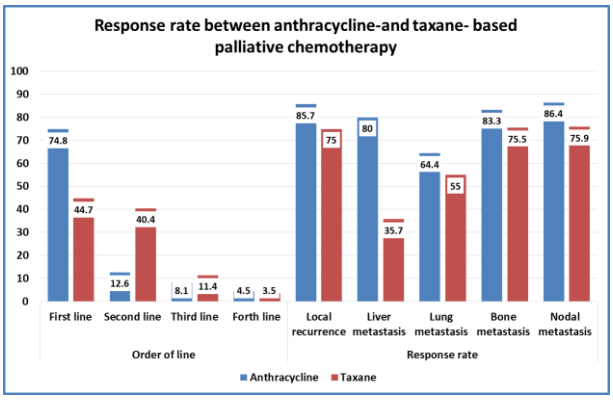

Figure 1 Response rate between anthracycline-based and taxane- based palliative chemotherapy on the studied MBC patients

Progression free and overall survival in the both regimens:

The 5 years OS was higher in the MBC patients who received taxane based regimen than the patients who received anthracycline based regimen (74.5 ± 5.2% vs 54.9 ± 6.5% P value 0.015) but there is no difference in the PFS in both groups as shown in Table 4.

Table 1 The baseline data of the studied BC patients (n=225)

Baseline data		Anthracycline (n=111)		Taxane (n=114)		P value
Age (years)	Mean ± SD	49.67 ± 11.75		49.69 ± 11.83		0.987
	Median (range)	49 (28 – 75)		49 (29 – 75)		
	≥50	55	(49.5)	56	(49.1)	0.949
	<50	56	(50.5)	58	(50.9)	
Menopausal status	Premenopausal	51	(45.9)	50	(43.9)	0.926
	Postmenopausal	47	(42.3)	49	(43.0)	
	Perimenopausal	13	(11.7)	15	(13.2)	
Tumor size	Early (T1+T2)	57	(51.4)	68	(59.6)	0.210
	Advanced (T3+T4)	54	(48.6)	46	(40.4)	
Positive Mets LNs	N0	7	(6.3)	17	(14.9)	0.160
	N1	22	(19.8)	22	(19.3)	
	N2	35	(31.5)	27	(23.7)	
	N3	47	(42.3)	48	(42.1)	
Primary site of metastasis at presentation	Nodal	28	(25.2)	18	(15.8)	0.079
	Liver	31	(27.9)	19	(16.7)	**0.043**
	Lung	40	(36.0)	26	(22.8)	**0.029**
	Bone	38	(34.2)	23	(20.2)	**0.018**
	Brain	1	(0.9)	1	(0.9)	1
	Local metastasis	73	(65.8)	46	(40.4)	**<0.001**
Histology	IDC	102	(91.9)	102	(89.5)	0.950
	ILC	2	(1.8)	3	(2.6)	
	Mixed	3	(2.7)	3	(2.6)	
	Others*	4	(3.6)	6	(5.3)	
Associated DCIS	Yes	32	(28.8)	36	(31.6)	0.653
	No	79	(71.2)	78	(68.4)	
Grade	Grade 2	99	(89.2)	96	(84.2)	0.272
	Grade 3	12	(10.8)	18	(15.8)	
Type of operation	MRM	49	(44.1)	65	(57.0)	0.096
	BCS	10	(9.0)	14	(12.3)	
	Tissue biopsy	46	(41.4)	32	(28.1)	
	Simple mastectomy	6	(5.4)	3	(2.6)	
Principle of operation	Curative	34	(30.6)	64	(56.1)	**0.001**
	Palliative	32	(28.8)	20	(17.5)	
	Diagnostic	45	(40.5)	30	(26.3)	
Surgical margins	Free	62	(55.9)	80	(70.2)	0.087
	Positive	3	(2.7)	2	(1.8)	
	Not applicable	46	(41.4)	32	(28.1)	
Lymphovasular invasion	Yes	53	(47.7)	62	(54.4)	0.075
	No	12	(10.8)	20	(17.5)	
	Not applicable	46	(41.4)	32	(28.1)	
Perineural invasion	Yes	21	(18.9)	24	(21.1)	0.100
	No	44	(39.6)	58	(50.9)	
	Not applicable	46	(41.4)	32	(28.1)	
Extracellular extension	Yes	20	(18.0)	24	(21.1)	0.107
	No	45	(40.5)	58	(50.9)	
	Not applicable	46	(41.4)	32	(28.1)	

BCS, breast conservative surgery; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; MRM, modified radical mastectomy; SD, standard deviation; Others include, Metaplastic carcinoma, Mets adenocarcinoma, Moderate differentiated adenocarcinoma, Poor differentiated adenocarcinoma, undifferentiated carcinoma.
Quantitative data are presented as mean ± SD and median (range), qualitative data are presented as number (percentage). P-value set significant at 0.05 level.

Table 2 Hormonal profile of the studied BC patients (n=225)

Hormonal profile		Anthracycline (n=111)		Taxane (n=114)		P value
Estrogen receptor	Negative	55	(49.5)	52	(45.6)	0.555
	Positive	56	(50.5)	62	(54.4)	
Estrogen receptor strength	Negative	55	(49.5)	52	(45.6)	0.906
	Weak	5	(4.5)	6	(5.3)	
	Moderate	27	(24.3)	32	(28.1)	
	Strong	24	(21.6)	24	(21.1)	
Progesterone receptor	Negative	67	(60.4)	61	(53.5)	0.299
	Positive	44	(39.6)	53	(46.5)	
Progesterone receptor strength	Negative	67	(60.4)	61	(53.5)	0.450
	Weak	10	(9.0)	15	(13.2)	
	Moderate	20	(18.0)	27	(23.7)	
	Strong	14	(12.6)	11	(9.6)	
Her2/neu	Positive	21	(18.9)	22	(19.3)	0.766
	Negative	50	(45.0)	56	(49.1)	
	Not applicable	40	(36.0)	36	(31.6)	
Molecular classification	Luminal A	12	(10.8)	9	(8.7)	**<0.001**
	Luminal B	43	(38.7)	54	(51.9)	
	Her2 enriched	15	(13.5)	13	(12.5)	
	Triple negative	24	(21.6)	28	(26.9)	
	Not applicable	17	(15.3)	0	(0.0)	

Her2/neu, Human epidermal growth factor receptor 2.
Qualitative data are presented as number (percentage). P-value set significant at 0.05 level.

Table 3 Type and site of metastasis among the studied BC patients (n=225)

	Anthracycline (n=111)		Taxane (n=114)		P value
Type of metastasis					**<0.001**
• Synchronous	75	(67.6)	48	(42.1)	
• Metachronous	36	(32.4)	66	(57.9)	
Site of metastasis					
• Local metastasis	83	(74.8)	69	(60.5)	**0.022**
• Distant nodal metastasis	47	(42.3)	52	(45.6)	0.621
• Distant liver metastasis	37	(33.3)	32	(28.1)	0.392
• Distant lung metastasis	50	(45.0)	51	(44.7)	0.963
• Distant bone metastasis	44	(39.6)	44	(38.6)	0.873

Qualitative data are presented as number (percentage). P-value set significant at 0.05 level.

Table 4 Progression free and overall survival among the studied breast cancer cases according to the received protocol (n=225)

	PFS (5 years)		OS (5 years)	
	Estimate ± SE	**P value**	**Estimate ± SE**	**P value**
Received protocol		0.655		**0.015**
▪ Anthracycline	36.3 ± 6.7%		54.9 ± 6.5%	
▪ Taxane	36.0 ± 5.5%		74.5 ± 5.2%	

OS, overall survival; PFS, progression free survival; SE, standard error.

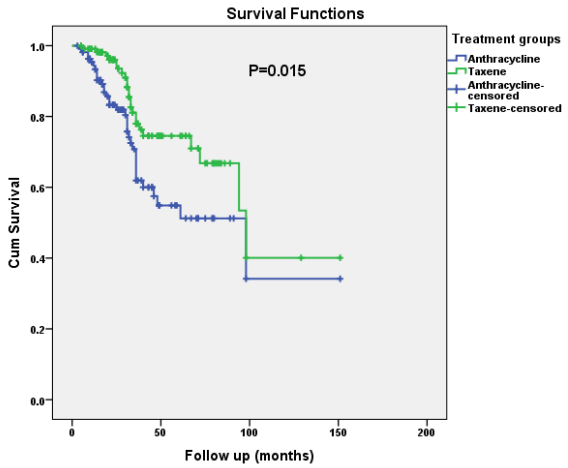

Figure 2 Kaplan Meier curve showing that taxane based regimen had the better OS than anthracycline based regimen.

Discussion:

Metastatic breast cancer is an incurable disease with main therapy purpose to increase patients' survival rate and to improve their quality of life. Accordingly, the key treatment should be to use the least toxic methods with safe and sufficient disease control [9].

In this study, we examined patients with metastatic breast cancer at Medical Oncology Department of South Egypt Cancer Institute, Assiut University in the interval between January 2013 to December 2018 to evaluate the efficacy of anthracycline based regimen compared to taxane based regimens as a palliative line therapy for MBC patients.

Clinicopathological criteria were nearly balanced between the two groups including age, menopausal status, tumor size, nodal status, distant metastasis, tumor grade, histo-pathological criteria, hormonal status and site of metastases.

The mean age of our patients at time of diagnosis was 49.67 with standard deviation of 11.75 years, which is similar to the study of Frank, Carton et al which stated the mean age of patients was a mean age of 51.3 years also in Azim, Elghazawy et al study with mean age of their reported cases was of 50.4 years at diagnosis time [24, 25].

The left breast was the most frequently affected at the presentation on both groups (who received anthracycline based and who received taxane based chemotherapy) (57.7%, 51.8%) respectively which was similarly mentioned in Seely and Alhassan study and Lester and Hicks [26, 27].

The most common histo-pathological type in both groups was infiltrating ductal carcinoma (91.9%, 89.5%) which was closely found in Gemici, Ozal et al study that was 88.75% [28] and this is already known as the universal most common pathological type.

Unlike the study by Kennecke et al, we reported that larger tumor size (T3/4) was significantly associated with the incidence of distant metastases [29]. The primary tumor size correlates with the prognosis of distant metastases, but there shows no significant correlation between the regional lymph node metastasis and the prognosis. These observations may reflect the impact of patient characteristics on the more aggressive disease tendencies.

In our study, the patients who received anthracycline based regimen were presented in a premenopausal stage (45.9%), and with a severe disease as they presented with IDC (91.9%) and high pTNM stage with advanced T (48.6%), N3 (42.3%) which was also stated in the study done by Guo, Yi et al with the patients who were with a severe disease (IDC, lymph node involvement, high pTNM stage, and shorter DFS) which represented the categories of patients more likely treated with anthracycline based regimens [30].

On the other hand, the patients who received taxane based regimen were presented with low risk features as they presented with early T (59.6%), and about sixty-four patients (56.1% P value 0.001) underwent curative surgery. These findings were compatible with Ueno, Masuda et al study and Maurya and Brahmachari study [31] [32].

Luminal type B was mutual in our patients on both groups than other types, it constituted about (38.7 %, 51.9 % with P value <0.001) when compared to luminal type A, HER-2 enriched, and triple negative which constituted (10.8%, 8.7%), (13.5%, 12.5%), (21.6%, 26.9%) respectively which agreed with Mohammed, Ayad Ahmad study in which luminal type B was about 43.73% while luminal type A, HER-2 enriched and triple negative were constituted 27.97%, 20.9%, and 7.4% respectively [33].

In contrast to, Rweyemamu, Akan et al which the luminal-A sub-type represents the most common subtypes among the studied population (44.5%) followed by luminal-B (22.4%), triple-negative (22.1%) and HER-2 enriched (11%) [34].

In our study, about eighty-three (74.8% with P value <0.001) patients received anthracycline based regimen as a first line palliative therapy while about fifty-one and forty-six (44.7%, 40.4%) patients received taxane based regimen as a first and second line therapy respectively which was also in agreement with Gradishar, Moran et al study and Moy, Rumble et al study [35] [36].

Among the MBC studied patients, the incidence of receiving anthracycline based regimen was higher as a first line palliative therapy than receiving taxane based regimen (74.8% vs 44.7% with P value <0.001) which was agreed with Chang, Wu et al study and with Feinberg, Kish et al study in which anthracycline based regimen more prescribed as a first line than taxanes (37.2% vs 14.3%) [37] [38] but was disagree with Wallrabenstein, Oseledchyk et al study which prescribed taxanes as a first line more than anthracycline based regimen [39].

While the incidence of receiving taxane based regimen was higher as a second line therapy than receiving anthracycline based regimen (40.4% vs 12.6%) which was agree with Anand, Niravath et al study [40] but was disagreed with Biganzoli, Battisti et

al study in which was more prescribed taxane based regimen to avoid cardiac toxicity from anthracycline based regimen [41].

In the patients with liver metastasis, we found a greater response rate in the patients who received anthracycline based regimen than the patients who received taxane based regimen (80.0% vs 35.7% P value <0.001) which was agree with Sharma, Kimler et al study in which the response rate was (54% vs 28%) [42].

The 5 years overall survival regimen show significant response in patients who received taxane based regimen in comparable to the patients who received anthracycline based regimen (74.5 ± 5.2% vs 54.9 ± 6.5% P value 0.015) respectively but no difference in PFS. These findings agree to Early Breast Cancer Trialists' Collaborative Group study which showed the median follow-up for taxane without anthracycline was only 5.4 years [43].

On the other hand, Hurvitz, McAndrew et al and Sharma, Kimler et al reported that no significant difference in OS between the two groups but reported improvement in PFS. These variation in the results may attributed to different methods for evaluation and interpretation [42, 44].

While in the study done by Nagasaki, Kudo et al, showed that improvement in OS and PFS in the patients who received anthracycline based regimen incomparable with the patients who received taxane based regimen (87%, 58% vs 28.3%, 26.7%) respectively, which was in contrast to our findings that were reported [45].

Anthracyclines and taxanes are commonly considered to be used as a first-line chemotherapy regimen in patients with MBC. the choice of treatment in these patients population should depend on not only on efficacy data but also on other factors such as patient performance status, the presence of comorbidities, patient personal preference, histological type and molecular subtype.

Limitations

As results presented in this study, the findings were not to be generalizable for all patients with MBC and visceral metastases. Sample sizes, particularly for triple negative and HER2+ subtypes of cases were small, which may have impacted the results. As with all observational, non-randomized, retrospective studies, unmeasured confounding may be present. Information on subsequent or combination therapies was not controlled for in our study, which could vary by the treatment and could potentially impact outcomes, particularly overall survival. Tolerability and adverse effects were not captured. However, despite the above-mentioned limitations, the present study also possesses strengths, such as a large and representative sample size, reliable data, and rigorous analyses; thus, it would be useful to describe the clinical use of anthracycline based versus taxane based regimen in metastatic breast cancer patients.

Conclusion:

Anthracycline based regimen shows significant response rate in patients with liver metastasis in comparable to taxane based regimen while the patients who received taxane based regimen show more significant OS but no difference in PFS in both groups.

Abbreviations

CR	Complete response
ECOG	Eastern Cooperative Oncology Group
Her2	Human epidermal growth factor receptor 2
IDC	Invasive ductal carcinoma
ILC	Infiltrating lobular carcinoma
MBC	Metastatic breast cancer
RR	Response rate
OS	Overall survival
PARPis	Polyadenosine diphosphate-ribose polymerase inhibitors;
PFS	Progression-free survival
PR	Partial response
SD	Stable disease
SD	Standard deviation
SE	Standard error
TNBC	Triple-negative breast cancer
BLBC	Basal like breast cancer
BCS	Breast conservative surgery
vs	Versus

Ethics approval and consent to participate

Our trial was approved by the ethics committee and institutional review board at the South Egypt Cancer Institute under the number of SECI-IRB No: 543. The committee was approved the research confirmed and all research was performed in accordance with relevant guidelines/regulations. The informed written consent was obtained from the all participants and/or their legal guardians. The drugs were supplied by governmental and health insurance at the location of the study.

Consent for publication

Oral consent for publication was obtained from patients participating in this study.

Competing interests

The authors declare that they have no competing interests.

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