

Comparative Study between Vinorelbine based Versus Taxanes based Chemotherapy in Treatment of Parenchymal Metastatic Breast Cancer

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Received date: May 03, 2016; Accepted date: June 18, 2016; Published date: June 28, 2016

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Abstract

Background: Vinorelbine based and taxanes based chemotherapy are the most commonly used regimens given for parenchymal metastatic breast cancer. This study was held to compare the response of those regimens according to Response Evaluation Criteria In Solid Tumors (RECIST) in patients with parenchymal metastatic breast cancer in Suez Canal University Hospital, Clinical Oncology and Nuclear Medicine Department (SCUCON).

Aim: We performed this study to identify the best management to be given for patients with parenchymal metastatic breast cancer in (SCUCON).

Patients and Methods: This was a retrospective descriptive study that included all the patients with parenchymal (lung and/or liver) metastatic breast cancer (166 patients) treated in SCUCON between Jan 1995 and Jan 2011. The collected data included the medical history, clinical, laboratory, radiological and pathological data, the treatment received and follow-up for each patient, from files which are coded. Data was recorded without identifiable information, so the researchers asked for waiving of informed consent because it is a retrospective study.

Results: The study included 166 representing 12.6% of breast cancer patients. Over all comparison showed mild superiority of Navalbine based chemotherapy over Taxanes based chemotherapy. In metastatic breast cancer to liver, complete response was 25% with Navalbine compared to 54.5% with Taxanes. While in metastatic breast cancer to lung, complete response was 40.9% with Navalbine compared to only about 9% with Taxanes.

Conclusion: Navalbine based chemotherapy is more superior in patients with metastatic breast cancer to lung, while Taxanes based chemotherapy is more superior in patients with metastatic breast cancer to liver.

Key words:

RECIST; Metastatic breast cancer; Treatment response; Chemotherapy

Introduction

Breast cancer is the most commonly diagnosed cancer among women and second only to lung cancer as the leading cause of cancer-related deaths in women, breast cancer occurs approximately 150 times more frequently in women than in men [1]. In the world, each year more than 1 million women are diagnosed with breast cancer and more than 400000 die from it [2]. The disease is very rare before the age of 20, seldom occurs below 30 years of age, and its incidence rate rises up to the age of 50 years. In postmenopausal women, the rate of increase slows down, although the incidence continues to rise [1,3]. Breast cancer represents 30% of cancer new cases in developed countries and 14% in developing countries [4]. In Egypt, data reported by the Gharbiah population based cancer registry (2001) indicated that breast cancer ranked first among females (37.6%), with an age-standardized rate of 49.6/100000. On the other hand, carcinoma of the male breast was only 0.5% [5]. In Egypt, breast cancer is the most common cancer among women, representing 18.9% of total cancer cases (35.1% in women and 2.2% in men) among the Egypt National

Cancer Institute (NCI) series of 10 556 patients during the year 2001 [6]. Metastatic breast cancer-MBC is not considered curable. Therefore, the goals of treatment must carefully balance the risks of treatment-induced toxicity with the expected clinical benefit [7]. Accepted clinical endpoints in the treatment of MBC include prolonged overall survival, improved quality of life, progression free survival, and cancer-related symptom control [8,9]. Most patients with MBC present with a recurrence following treatment for early stage breast cancer. Less than 10% of patients present with MBC at the time of initial diagnosis [9]. The most common sites of metastatic recurrence are bone, lungs, liver, and the central nervous system and up to 50–75% of patients with MBC will have single organ involvement [10]. Selection of initial and subsequent treatment requires consideration of multiple factors [8-11].

- Intent of treatment.
- Estrogen receptor (ER), progesterone receptors (PR), and human epidermal growth factor receptor- 2 (HER's-2) statuses.
- Sites of disease.
- Co-morbid conditions.
- (ECOG) Eastern Cooperative Oncology Group
- Performance status of the patient
- Toxicities of treatments.

- Pace of disease progression.
- Previous treatment and responses.
- Need for concurrent localized therapy (e.g., radiotherapy or surgery for bone or CNS disease).

Several prognostic factors contribute to predicting an individual patient's course of disease [1]. Prolonged relapse-free survival of more than 5 years is more favourable. Isolated chest wall or ipsilateral nodal recurrence predicts better outcome than visceral disease. Bone and soft-tissue recurrence is more favourable than parenchymal or central nervous system disease. The prognostic value of HER-2 status on MBC, especially with the adjuvant of Trastuzumab and Lapatinib is not established. Up to 2-3% of patients with favourable characteristics may be long-term survivors with over 20-year survival. Such patients tend to be young, have limited disease, and have a complete response to initial therapy. Endocrine therapy is preferred for most patients with hormone receptor positive and non-life threatening parenchymal metastasis [12]. The following general guidelines applies to selection of hormonal therapy for MBC [12-14].

Endocrine therapy should be initial treatment for patients with hormone receptor positive tumors without symptomatic visceral metastases or rapidly progressive disease [12-14]. The response rates to hormonal therapy for ER+/PR+, ER+/PR-, ER-/PR- are 70%, 40%, and 10%, respectively [12-14]. Patients with primary endocrine resistance generally should proceed directly to chemotherapy [12,13]. The following are guidelines for chemotherapy treatment in MBC [15-17].

Patients with visceral metastases, rapidly progressive disease, or hormone refractory disease may be treated with chemotherapy. First-line chemotherapy results in response rates of 30-60% and improved quality of life (Table 1).

Doxorubicin 60 mg/m ² IV..... every.....	..21 days
Doxorubicin 20 mg/m ² IV	every..... 7 days
Paclitaxel 175 mg/m ² IV	every..... 21 days
Paclitaxel 80 mg/m ² IV..... every.....	7 days
Docetaxel 100 mg/m ² IV.....every.....	21 days
Docetaxel 40 mg/m ² IV	every.....7 days
Vinorelbine 30 mg/m ² IV	every.....7 days
Capecitabine 1,250 mg/m ²	
PO twice daily days 1-14.....every.....21 days

Table 1: Single Agent Chemotherapy Regimens for Metastatic Breast Cancer [16-18].

Combination chemotherapy has higher response rates but more toxicity [18]. Paclitaxel and docetaxel may be given on weekly or every three-week schedules. Response rates may be higher with weekly dosing, but overall survival is similar and neurotoxicity is significantly worse. Patients who progress on paclitaxel may respond to docetaxel. Docetaxel is also active as first-line therapy but supportive measures should be considered for patients with an ECOG performance status -3 or after lack of response to three successive single agent chemotherapy regimens [1-19]. Vinorelbine based and Taxanes based chemotherapy are the most commonly used regimens given for parenchymal metastatic breast cancer [17]. This study was held to compare the response of those most commonly used regimens (Vinorelbine vs.

taxanes) according to Response Evaluation Criteria In Solid Tumors (RECIST) in patients with parenchymal metastatic breast cancer in Suez Canal University Hospital, Clinical Oncology and Nuclear Medicine Department [8,9].

Patients and Methods

Study location

The study was conducted at Suez Canal University Hospital, Clinical Oncology and Nuclear Medicine Department (SCUCON), Ismailia, Egypt between January 1995 and January 2011.

Inclusion criteria

- Patients with parenchymal (lung and/or liver) metastatic breast cancer treated in the department of clinical oncology and nuclear medicine between Jan.1995 and Jan. 2011 are included in the study.
- Patients with ECOG performance status 0-2.
- Patients received at least 3 cycles of either Vinorelbine based or taxanes based chemotherapy as first line after appearance of metastasis.

Exclusion criteria

- Patients with non-metastatic breast cancer.
- Patients with other visceral metastasis (brain, local recurrence or other soft tissue recurrence).
- Patients with parenchymal (lung and/or liver) metastatic breast cancer from the start.
- Patients with metastatic breast cancer to bone as a sole site of metastasis.
- Patients with other malignancies (sarcoma or lymphoma) of the breast.

Study design

This was a retrospective descriptive study that the required data were collected from the file recording system of (SCUCON). In this system, the personal, clinical, laboratory, radiological, pathological, management and follow-up data for each patient were recorded in a separate file.

Personal history

This includes age at diagnosis, gender, age of menarche and menopause, address, occupation, and date of presentation.

Patient's main complaint

The most distressing symptoms (palpable mass, pain, weight loss etc).

Present history

(Onset of symptoms, Course of symptoms, duration of symptoms before presentation, presence of other co morbidities),

History of chronic illness

Past history: Past history of same cancer or other types of cancers.

Family history: Same cancer or other types of cancers.

Examination

- General examination.
- Local examination.
- Eastern Cooperative Oncology Group (ECOG) performance status
- 0–Asymptomatic (Fully active, able to carry on all predisease activities without restriction)
- 1–Symptomatic but completely ambulatory (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. For example, light housework, office work)
- 2 – Symptomatic, <50% in bed during the day (Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours)
- 3–Symptomatic, >50% in bed, but not bedbound (Capable of only limited self-care, confined to bed or chair 50% or more of waking hours)
- 4–Bedbound (Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair)
- 5–Death

Investigations

- Laboratory (complete blood picture, liver function test, renal function test, tumor marker CA15-3)
- Radiological assessment at initial presentation, during follow up and after chemotherapy (X-ray, ultrasound, computerized tomography-CT or magnetic resonance imaging- MRI).

The management received at Hospital

- Surgery, hormonal treatment, radiotherapy or chemotherapy.
- Pathological type and grade.
- Staging; TNM staging system.

The response of chemotherapy given for Patients with parenchymal metastatic breast cancer was evaluated according to Response Evaluation Criteria In Solid Tumors (RECIST) from the filing record of pre and post chemotherapy imaging (X-ray, ultrasound, CTs or MRI) and also tumor marker's difference as follows:

Complete response (CR): Disappearance of all target lesions.

Partial response (PR): At least a 30% decrease in the sum of the longitudinal diameter LD of target lesions, taking as reference the baseline sum LD.

Stable disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started.

Progressive disease (PD): At least a 20% increase in the sum of the LD of target lesions, taking as reference the smallest sum LD recorded since the treatment started or the appearance of one or more new lesions.

Statistical analysis

Data was analyzed using the Statistical Package of Social Science (SPSS). Version 15 (SPSS Inc., Chicago, L, USA).

Data entry and analysis by using the “SPSS 15.0” by aid of the following statistical tests:

Continuous variables are presented as means ± standard deviation (SD).

Discrete variables are expressed as frequencies and percentages.

Chi square and the Fishers exact test were used to test significance of the difference between qualitative data.

Probability value (P) <0.05 is considered statistically significant.

Presentation of the statistical outcomes and tables was performed using the “Microsoft Word 2007” program.

Results

Between January 1995 and January 2011:7462 patients were treated in the department of clinical oncology and nuclear medicine in Suez Canal university hospital not including those referred from the health insurance. The number of patients diagnosed to have breast cancer during the same period is 941 patients (12.6%), and from these patients 166 patients (17.6%) were diagnosed to have liver and lung metastatic or breast cancer. The majority of patients (about 99%) were females, the minimum age at diagnosis was 28 years old, the maximum is 67 years old and the peak age was between 38-48 years old. The mean disease free interval was 2.37 years old and 61.4% of the patients after appearance of parenchymal metastasis received Navalbine based chemotherapy, while 38.6% received Taxanes based chemotherapy. Over all comparison between Navalbine based chemotherapy *v/s* Taxanes based chemotherapy response in treatment of parenchymal metastatic breast cancer revealed that 31.4% of patients received Navalbine showed complete response compared to 25% of patients received Taxanes. Which is statistically insignificant (Figure 1).

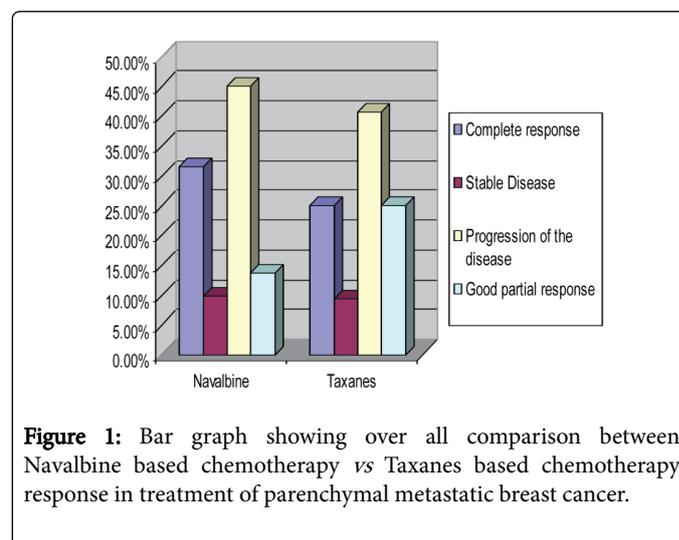
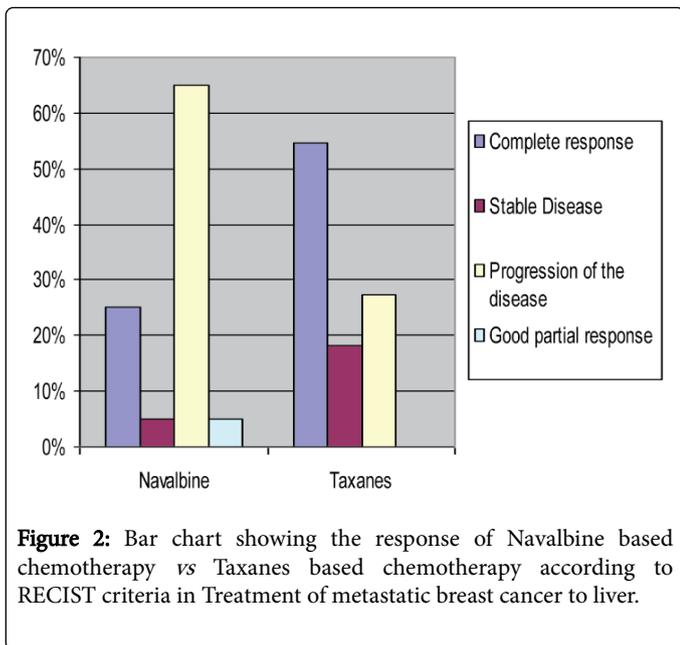
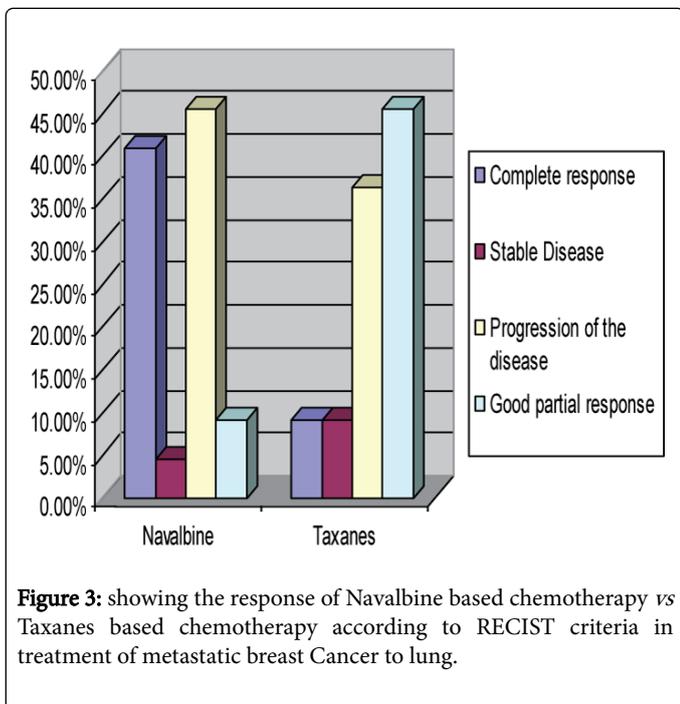


Figure 1: Bar graph showing over all comparison between Navalbine based chemotherapy *vs* Taxanes based chemotherapy response in treatment of parenchymal metastatic breast cancer.

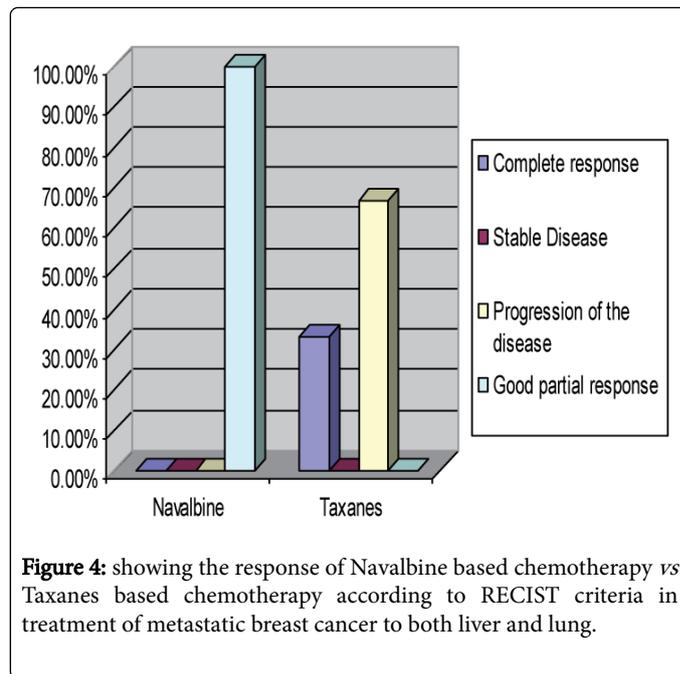
Comparing the response of Navalbine based chemotherapy *v/s* Taxanes based chemotherapy according to RECIST criteria in treatment of metastatic breast cancer to liver (n=62); 25% patients who received Navalbine attained complete response compared to 54.5% of patients who receive Taxanes and 65% of those who received Navalbine developed progression of the disease compared to 27.3% of patients who received Taxanes which is statistically significant (Figure 2).



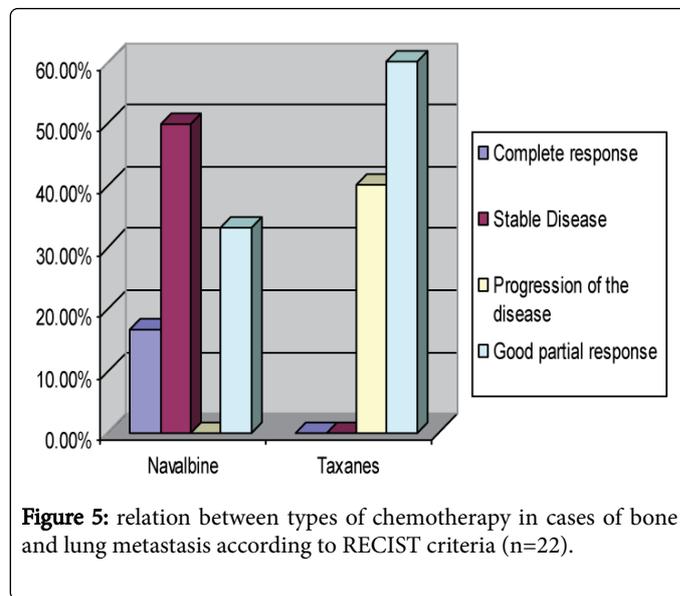
Comparing the response of Navalbine based chemotherapy v/s Taxanes based chemotherapy according to RECIST criteria in treatment of metastatic breast cancer to lung (n=66) revealed; about 41% patients who received Navalbine attained complete response compared to 9.1% of patients who receive Taxanes which is statistically significant (Figure 3).



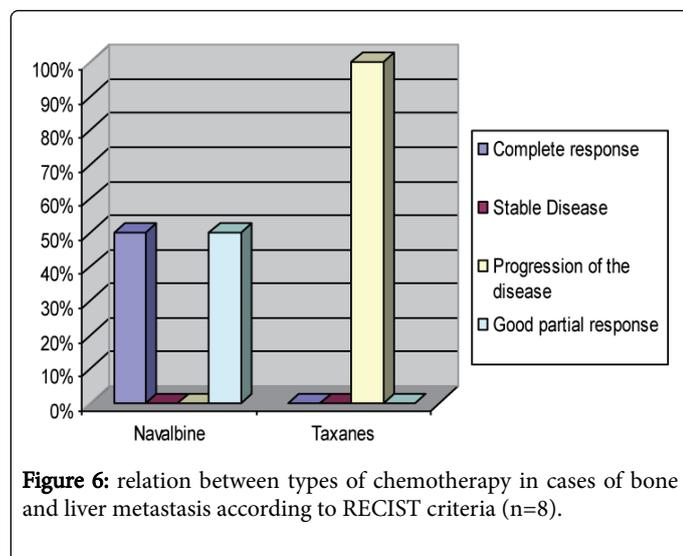
The response of Navalbine based chemotherapy v/s Taxanes based chemotherapy in treatment of metastatic breast cancer to both liver and lung was; 33.3% patients who received Taxanes attained complete response compared to 0% of patients who receive Navalbine which is statistically significant as shown in (Figure 4).



In metastatic breast cancer to both bone and lung (n=22); 16.7% patients who received Navalbine attained complete response compared to 0% of patients who receive Taxanes which is statistically significant as shown in (Figure 5).



In metastatic breast cancer to both bone and liver (n=8); 50% patients who received Navalbine attained complete response compared to 0% of patients who receive Taxanes which is statistically significant as shown in (Figure 6).



Discussion

In this retrospective study we found that; in Suez Canal University center of Oncology and Nuclear Medicine (SCUCON), the total number of cases diagnosed to have breast cancer from January 1995 to January 2011 is (941 patients) representing (12.6%) of the total number of patients (7462 patients totally) presented to the unit during the same period of time which is in agreement with the Egyptian National Cancer Institute -NCI- (2002) which reported that; in Egypt, breast cancer is the most common cancer among women, representing 18.9% of total cancer cases presented to (NCI)[6]. Regarding Age, our study revealed that our patients were in the age group ranging from 28 to 67 years old, and the mean age of the studied patients was 48.05 years old and the peak age of diagnosis is around 50 years old, and also (58.5%) of the female patients were postmenopausal women and all this was in agreement with the studies done by Berry DA which stated that the disease is very rare before the age of 20, seldom occurs below 30 years of age, and its incidence rate rises up to the age of 50 years and in postmenopausal women, the rate of increase slows down, although the incidence continues to rise [2]. The disease free interval between initial diagnosis of breast cancer and appearance of metastasis: In our search there were about (35) patients diagnosed to have metastatic breast cancer from the start representing (3.7%) of total number of cases of breast cancer- who are not included to our study because they received anthracycline based rather than Vinorelbine based or Taxanes based chemotherapy and also our study reported that the time interval between diagnosis of breast cancer and appearance of metastasis is two years in about (60%) of cases.

Coleman [19], stated that less than 10% of patients present with metastatic breast cancer at the time of initial diagnosis and also Moysich [20] documented that the probability of occurrence of metastasis is highest within the first 5 years after diagnosis of breast cancer. So our study is nearly in agreement with this study [19,20]. Regarding response of Navalbine based chemotherapy *v/s* Taxanes based chemotherapy in treatment of parenchymal metastatic breast cancer; the frequency distribution of patients with parenchymal (lung and/or liver) metastatic breast cancer according to site of metastasis was as follows: About 40% of the patients had lung metastasis as a sole site of metastasis, 37.3% of the patients had liver metastasis as a sole site of metastasis, 4.8% had metastasis to both lung and liver, 13.3%

lung and bone metastasis and 4.8% had metastasis of liver & bone. Of those patients 61.4% of the patients after appearance of parenchymal metastasis received Navalbine based chemotherapy, while 38.6% received Taxanes based chemotherapy.

Over all comparison between Navalbine based chemotherapy *v/s* Taxanes based chemotherapy response in treatment of parenchymal metastatic breast cancer revealed that: Patients who received Navalbine, 31.4% showed complete response and about 14% showed partial response. Compared to Patients who received Taxanes, 25% showed complete response and about 25% showed partial response.

This is in agreement with Sparano [21] who stated that the use of Taxanes in treatment of metastatic breast cancer gives response rate 35-55% a Martin [22] and Byron [23] who documented that Vinorelbine immunotherapy in patients with advanced or MBC has produced widely varying results, with response rates ranging from 25% to 46% [21]. While according to Vassilomanolakis [24] the use of Vinorelbine in combination with cisplatin increases the response rates in the range of 40%-50% [22-24]. If we talk in details, we find that; Navalbine is more superior in patients with metastatic breast cancer to lung, while Taxanes are more superior in patients with metastatic breast cancer to liver as follows: In patients with metastatic breast cancer to liver, 25% patients who received Navalbine showed complete response compared to 54.5% of patients who receive Taxanes. In patients with metastatic breast cancer to lung, 40.9% patients who received Navalbine showed complete response compared to only about 9% of patients who receive Taxanes.

Conclusion

From this study we concluded that Breast cancer is a frequent malignancy among patients presented to Suez Canal University center of Oncology and Nuclear Medicine (SCUCON) and represent (12.6%) of all malignancies. 17.6% of patients who were diagnosed to have breast cancer developed parenchymal (liver and/or lung) metastatic breast cancer and included in our study. Navalbine based chemotherapy is found to be more superior in patients with metastatic breast cancer to lung, while Taxanes based chemotherapy is found to be more superior in patients with metastatic breast cancer to liver. The cost difference between Navalbine and taxanes together with its proper selection for treatment of parenchymal metastatic breast cancer; will result in considerable Cost Benefit for patients and government.

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