

# Work Productivity and Activity Impairment in Breast Cancer Patients Treated with Capecitabine

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## ABSTRACT

**Background:** Although the majority of breast cancer patients are able to work, lower work ability and reduced job retention have been reported. The aim of the present study was to evaluate the effect of chemotherapy with capecitabine in patients with breast cancer on work productivity and daily activity. **Methods:** 34 patients with metastatic breast cancer were enrolled for our study. Capecitabine was given twice daily at a cumulative dose of 2500 mg/m<sup>2</sup> on days 1 - 14 and repeated on day 22. Work productivity was determined using the WPAI questionnaire. **Results:** We observed an increase in absenteeism, presenteeism, work productivity loss and daily activity impairment after 1 cycle and 6 cycles of therapy, but we could not find statistically different significances. **Conclusions:** This study provides some data indicating an association between problems in breast cancer and work. Our results confirm that capecitabine may improve quality of life of patients with metastatic breast cancer.

**Keywords:** Breast Cancer; Capecitabine; Work Productivity; Absenteeism; Presenteeism

## 1. Introduction

Breast cancer is one of the most frequently diagnosed cancer as well as a leading cause of cancer mortality in women. A growing proportion of women diagnosed with breast cancer, present with earlier disease stages. Approximately 50% of all women diagnosed with breast cancer develop metastatic disease, and for these patients the average survival time from the time of diagnosis of metastatic disease ranges from 20 to 36 months. After surgery, the next question always is the need for adjuvant treatment and also the choice of chemotherapeutic agent. The goal of systemic therapy in early breast cancer is to eradicate micrometastases and reduce the risk of recurrence and death.

Capecitabine is an innovative fluoropyrimidine carbamate, developed as an orally administered precursor of 5'-deoxy-5 fluorouridine [1]. Capecitabine is an effective, well tolerated, and convenient treatment for patients with breast cancer. Along a pathway with three enzymatic steps, capecitabine is finally converted into the active

compound 5-FU at the site of tumor tissue, by the tumor-associated angiogenic factor thymidine phosphorilase, which is overexpressed in tumor cells [2]. The oral formulation and the rarity of alopecia make capecitabine a very acceptable and suitable drug, particularly for metastatic disease, because it is associated with a better quality of life than intravenous therapies [3]. Although the majority of breast cancer patients are able to work, lower work ability and reduced job retention have been reported [4,5]. The aim of the present study was to evaluate the effect of chemotherapy with capecitabine in patients with breast cancer on work productivity and daily activity.

## 2. Methods

Between January 2011 and February 2013, female patients with metastatic breast cancer that desired to continue their job were recruited for postoperative adjuvant oral chemotherapy with capecitabine. The study protocol was approved by the Institutional Review Board. Written informed consents were obtained from all participants.

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Further eligibility criteria included the following: 1) Age 30 to 50 years; 2) Eastern Cooperative Oncology Group performance status of 0 or 1; 3) Adequate hematological function (absolute leukocyte count 4000 to 12,000 leukocytes/mm<sup>3</sup>; neutrophil count 2000 neutrophils/mm<sup>3</sup> or more, and platelets 100,000/mm<sup>3</sup> or more) hepatic function (transaminases 2.5 times or less the upper limit of normal and serum bilirubin 2.0 mg/dl or less) and renal function (serum creatinine below the upper limit of normal); 4) Ability to take oral medication. Patients were excluded if they had any of following: history of severe drug allergies, interstitial pneumonitis or pulmonary fibrosis, several pleural effusion or ascites, active infection, diarrhea or serious uncontrolled comorbidities or medical conditions. Patients were also excluded if they were participating in another trial, unwilling to use effective contraception or had a medical condition or concomitant illness that might impair protocol compliance. Patients had received no prior chemotherapy. Capecitabine was given twice daily at a cumulative dose of 2500 mg/m<sup>2</sup> on days 1 - 14 and repeated on day 22. The total daily dose was divided into two equal amounts and given roughly 12 h apart and within 30 min after a meal, usually breakfast and dinner. Baseline assessment were medical history, clinical examination, complete haematology with differential leucocyte count, clinical chemistry including coagulation parameters, tumour markers CA 125 and CA 19-9, chest radiography and computed tomographic scans of the abdomen, pelvis and chest before starting treatment at baseline.

### 2.1. Laboratory Exams

A complete routine chemistry including red cell count, hemoglobin, white cell count, platelets, prothrombin time, fasting plasma glucose, insulin, C-reactive protein, blood urea nitrogen, serum creatinine, bilirubin, ALT, aspartate aminotransferase, alkaline phosphatase,  $\gamma$ -glutamyl transpeptidase, and creatin phosphokinase levels was performed at every medical visit. All patients were included in the safety and efficacy analyses. The severity of the adverse effects was evaluated according to the National Cancer Institute Common Toxicity Criteria (NCI-CTC) version 2.0 [6].

### 2.2. WPAI (Work Productivity and Activity Impairment)

Work productivity was determined using the WPAI questionnaire. Patients reported the number of actual hours worked, hours missed due to chemotherapy, as well as the effect on productivity while working and doing regular activities during the past 7 days. The WPAI was self-administered and consisted of four questions that elicited employment status. Scores for absenteeism, presenteeism, overall work productivity loss and impairment in regular (non work) daily activities, such as work around the house, shopping, child care, exercising, studying, were derived as follows: Absenteeism = hours missed/hours missed + hours worked; Presenteeism = scale score/10; Work productivity loss = absenteeism + (hours worked  $\times$  presenteeism); Daily activity impairment = scale score/10. Score were transformed into percentage with higher percentages indicating greater work impairment, lower productivity and daily activity impairment [7].

### 2.3. Statistical Analysis

Results are expressed as means  $\pm$  standard deviations. Comparisons of quantitative data were made using the Student's t-test or Mann-Whitney test. Qualitative data were analyzed using the chi-square test. A P value of  $< 0.05$  was considered as indicating a statistically significant difference. All data management and statistical calculations were performed using SPSS 15.0 statistical package (Chicago, IL).

## 3. Results

Patients' characteristics at baseline are reported in **Table 1**. Blue collars (manual labourers) were 64% and white collars (non manual/office labourers) were 35%. The oestrogen receptor status was positive in 25% of patients, negative in 41%, unknown in 23%. 58% of patients had one metastatic site, while 41% had two metastatic sites. With regard to WPAI score, we observed an increase in absenteeism, presenteeism, work productivity loss and daily activity impairment after 1 cycle and 6 cycles of therapy, but we could not find statistically different significances (**Table 2**). Adverse events after 24 weeks chemotherapy included gastrointestinal toxicity: 5 (14%) patients had nausea, 4 (11%) vomiting, 7 (20%) diarrhoea, 4 (11%) mucositis, 6 (17%) stomatitis, 2 (5%) abdominal pain and 1 (2%) proctitis and higher rates of hand-foot skin reactions (12 patients, 35%). 20 (58%) patients showed fatigue (**Table 3**).

## 4. Discussion

Extensive clinical investigation has established that the standard 3-week cycle of capecitabine prolongs the time to disease progression, with similar or prolonged overall survival in patients with metastatic breast cancer. The possibility of staying at home instead of receiving treatment in hospital represents an important role on decision for many patients impacting less on quality of life and offering greater freedom [8]. This preference has influenced the adoption of oral capecitabine into the treatment of breast cancer [9]. The goal of this study was to evaluate the possible effects of chemotherapy stress on work

**Table 1. Patients' characteristics at baseline.**

Parameter	
N	34
Age range (years)	32 - 49
Heart rate (beats per minute)	86
SBP (mmHg)	130 ± 14
DBP (mmHg)	84 ± 9
BMI (kg/m <sup>2</sup> )	26.4 ± 4.1
Histological grade	
I	3 (8%)
II	15 (44%)
III	10 (29%)
Unknown	6 (17%)
Blue collars (manual labourers)	22 (64%)
White collars (non manual/office labourers)	12 (35%)
Oestrogen receptor status	
Positive	12 (35%)
Negative	14 (41%)
Unknown	8 (23%)
Number of metastatic sites	
1	20 (58%)
2	14 (41%)

**Table 2. WPAI score in patients with breast cancer (mean ± SD).**

	Baseline	After 1 cycle treatment	After 6 cycles treatment	Follow up
Absenteeism	3.9 ± 3.4	4.2 ± 3.5*	4.4 ± 3.9*	4.1 ± 3.8*
Presenteeism	30.2 ± 10.2	32.4 ± 11.4*	34.1 ± 14.1*	32.1 ± 12.1*
Work productivity loss	30.4 ± 12.8	32.4 ± 11.2*	34.8 ± 12.5*	31.6 ± 12.7*
Daily activity impairment	41.8 ± 15.1	43.6 ± 14.5*	44.8 ± 16.3*	42.8 ± 15.9*

Comparison with baseline: P = NS\*; P < 0.05\*\*; P < 0.001\*\*\*.

ability. The diagnosis and treatment of cancer can lead to side effects, late effects and psychological distress that reduce the mental and physical health. Capecitabine administered as monotherapy is a reasonable choice when single-agent chemotherapy is entertained as a treatment option for metastatic breast cancer. Toxicities are generally manageable, even for more frail patients. Work is often related to having a purpose in life, a sense of contributing and a distraction [10]. In employees with breast cancer, psychological and health-related distress is associated with poorer outcomes such as higher work limitations, higher presenteeism, and lower workplace support. In our patients treated with capecitabine we did not observe statistically different significances in absenteeism, presenteeism, work productivity loss and daily activity impairment after 1 cycle and 6 cycles of therapy. Work plays an important role in the psychological treatment for many patients; in fact the level of satisfaction at work was often stated as a strong motivator for social status

**Table 3. Toxic effects in treated patients according to NCI-CTC.**

	After 3 weeks chemotherapy		After 24 weeks chemotherapy	
	Grade 1 - 2	Grade 3 - 4	Grade 1 - 2	Grade 3 - 4
<b>Laboratory</b>				
Lowered haemoglobin	1	0	2	1
Lowered leucocytes	0	0	2	1
Lowered platelets	0	0	1	0
Raised creatinine	0	0	0	0
Raised bilirubin	0	0	0	1
<b>Gastrointestinal</b>				
Nausea	2	1	3	2
Vomiting	1	1	3	1
Diarrhoea	2	1	4	3
Mucositis	2	1	2	2
Stomatitis	2	1	4	2
Abdominal pain	0	0	2	0
Proctitis	0	0	1	0
<b>Others</b>				
Fatigue	4	3	10	10
Anorexia	1	1	2	0
Alopecia	0	0	0	0
Hand-foot skin reaction	6	4	10	2

and for social contacts. We think that cancer patients should be encouraged to resume their activities as soon as possible, especially when adverse events are few and tolerable. Symptoms and well-being interact; the improvements of treatment adherence and the low toxicity permitted our patients to resume their work again. If work stress is becoming too high this may result in negative consequences for job performance and possibly the development of diseases. Cancer diagnosis and treatment are associated with frailty and vulnerability [11,12]. Productivity loss due to absenteeism is often taken into account in economic evaluations that adopt a societal perspective and is measured simply by counting the number of days off work; measuring productivity loss due to presenteeism, on the other hand, is more complex. In fact, the evaluation of presenteeism requires the estimation of a normal productive output for a given role, after which the impairment in productive output may be quantified [13]. Reduction in symptoms reduces absenteeism, but its impact on presenteeism is more uncertain [14,15]. Depression affects productivity differently depending on the occupational status, with various aspects of productivity more typically impaired in different professions [16]. The most prevalent symptoms in breast cancer treated with chemotherapy include fatigue, cognitive limitations, distress, sleep disturbance, hand-foot skin reaction. This symptom was mostly present in blue collars, while fatigue was present in both blue and white collars. The results of this study confirm that the use of highly active, oral drugs with good tolerability is vital and may im-

prove quality of life. This study provides some data indicating an association between problems in breast cancer and work. It is unclear whether those who left the workplace would have remained at work if the problems related to cancer and its treatment were effectively addressed.

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