Quality of life and psychological reactions in women on first line chemotherapy for metastatic breast cancer. Correlations to tumour response and predictive factors

LIST OF PAPERS

This thesis is based on the following four papers, which are referred to in the text by their Roman numerals.

I. Svensson H, Einbeigi Z, Johansson H, Hatschek T, Brandberg Y.
Quality of life in women with metastatic breast cancer during nine months after randomization in the TEX trial (epirubicin and paclitaxel w/o capecitabine)
Breast Cancer Research Treatment 2010; 123(3):785-793.

II. Svensson H, Einbeigi Z, Johansson H, Hatschek T, Brandberg Y.
Health related quality of life as prognostic factor for response, progression-free survival and survival in women with metastatic breast cancer.
Medical Oncology, in press 2011

III. Svensson H, Brandberg Y, Hatschek T, Skrtic S , Enerbäck C, Einbeigi Z.
Specific single nucleotide polymorphisms as predictor of toxicity at chemotherapy in women with metastatic breast cancer and its association with health-related quality of life.
Submitted for publication

IV. Svensson H, Brandberg Y, Einbeigi Z, Hatschek T, Ahlberg K.
Psychological reactions to progression of metastatic breast cancer –
an interview study. *Cancer Nursing 2009; 32(1):55-63*

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ABSTRACT

Background: Health-related quality of life (HRQoL) is an important endpoint in clinical trials and as an aspect that must be considered in the treatment of patients with metastatic breast cancer. Treatment efficacy and toxicity are important factors for HRQoL, so it is imperative to study the effects of oncological treatment in terms of HRQoL. Different individuals experience different side effects, and genetic variation may affect the metabolism of certain chemotherapy drugs. Single nucleotide polymorphism (SNP) is the most common type of genetic variation in the human genome, and studies have shown that functional genotypes may be an underlying cause of severe chemotherapy toxicity. Prognostic factors are used to choose adequate treatment for the patient. Previous studies of metastatic breast cancer have shown that HRQoL data can predict response, time to progression, and survival. We have only limited knowledge of how patients experience their situation at the point of disease progression after first-line chemotherapy, and so there is a need to further investigate this area in order to better understand and support women with advanced-stage disease.

Aim: All four studies in this thesis were based on the TEX study. The aim was to study HRQoL and psychological reactions in women with metastatic breast cancer receiving chemotherapy. HRQoL was investigated as a prognostic factor for tumour response, progression-free survival, and overall survival; and the relationship between HRQoL, toxicity, and selected biological variations (SNPs) was also examined.

Patients and methods: In the TEX trial, 287 patients with locally advanced or distant metastatic breast cancer were randomized to either epirubicin and paclitaxel (ET) or epirubicin, paclitaxel, and capecitabine (TEX). Treatment was repeated every three weeks. HRQoL was assessed by the EORTC-QLQ C30 and EORTC QLQ-BR23 questionnaires at five points during nine months. Both quantitative (studies I-III) and qualitative (study IV) methods were used. Study I included 163 patients who answered the questionnaire at all five assessment points. Linear regression analysis was used to examine differences in HRQoL between the two groups, over time, and interactions between group and time. Study II included 252 patients who answered the questionnaire before randomization. Logistic regression analysis was used to examine whether HRQoL could be an independent prognostic factor for response to treatment, progression-free survival, and overall survival. Study III included 185 patients who answered the questionnaire at the two-month assessment and provided blood samples for the genotyping analyses. Multiple regression analysis was conducted to investigate if there were any correlations between HRQoL and toxicity, specific SNPs and toxicity, and SNPs, toxicity, and the impact on quality of life. Finally, Study IV was based on interviews with 20 patients; content analysis was used to analyse the data.

Results:

Study 1: At nine months, the groups showed a statistically significant difference in overall quality of life and physical function, in favour of patients treated with TEX. There were no other differences or interactions between the treatment groups.

Study II: Fatigue was correlated with response to treatment and overall survival. There were also associations between several variables and response (role functioning, social functioning, nausea and vomiting, and anorexia). The analysis showed no association between HRQoL and progression-free survival.

Study III: Statistically significant associations were found between several of the HRQoL variables and toxicity (fatigue, pain, dyspnoea, cardiovascular problems, gastrointestinal problems, and skin problems). Toxicity was also associated with specific SNPs that may affect the metabolism of the drugs used in the TEX trial. There is a connection between SNPs, toxicity, and HRQoL.

Study IV: Many of the women had suspected that their cancer was progressing. Worry was the most common reaction. The women had many different strategies to deal with the situation, and the majority of them understood and accepted their situation. Interest in professional counselling was small, and many reported that they felt that their first relapse was more traumatic.

Conclusion: HRQoL over time provides information that can be used in the choice of treatment, especially if no difference can be demonstrated in treatment response between the chosen treatments. Frequent quality of life measurements at different times give increased knowledge of patients' needs, allowing practitioners to better provide support and care during the course of disease. The analysis showed a relationship between fatigue and response to treatment and overall survival. The results also show that as patients' progress through treatment, they develop resources to deal with difficult information and do not necessarily express a need for professional psychosocial support. The analyses revealed an association between HRQoL and toxicity, between specific SNPs and toxicity, and between SNPs, toxicity, and the impact on quality of life. Such knowledge may influence the choice of chemotherapy in this patient population, depending on the treatment's toxicity profile and its impact on patients' quality of life.