ELSEVIER

Critical Reviews in Oncology/Hematology 65 (2008) 223–234

CRITICAL REVIEWS IN
Oncology
Hematology
Incorporating Geriatric Oncology

www.elsevier.com/locate/critrevonc

Implications of applied research for prognosis and therapy of breast cancer

M.F. Barginear, T. Bradley, I. Shapira, D.R. Budman *

Don Monti Division of Medical Oncology/Division of Hematology, North Shore University Hospital, New York University School of Medicine, United States

Accepted 30 November 2007

Contents

Abstract

Breast cancer is the one of leading causes of cancer-related deaths in women within economically developed regions of the world. The heterogeneity of the natural history of breast cancer complicates patient management in that there is tremendous variability in response to treatment and for survival. More recently, several biomarkers (hormone receptor status and HER2 expression) have been added to the risk evaluation and therapeutic assessments. Evolving knowledge of molecular biology and newer techniques, such as genomics and proteomics, offer the potential to better define the biologic nature of the disease process, both for risk and therapy. This review discusses classical as well as new prognostic and predictive techniques. These are leading to a paradigm shift from empirical treatment to an individually tailored approach, which may soon become a realistic option for patients, based on specific molecular profiles.

Keywords: Breast cancer; Molecular profiling; Gene expression profiles

1. Background

Each year, the American Cancer Society estimates the number of new cancer cases and deaths expected in the United States within the current year and compiles the most recent data on cancer incidence, mortality, and survival. Approximately, 180,000 new cases of invasive breast cancer will be diagnosed in 2007, and of these new cases, over 41,000 women will be expected to die of their disease [1]. Breast cancer is one of leading causes of cancer-related deaths in women within economically developed regions of the world; the lifetime risk of developing invasive breast cancer is 12.6% (one out of eight women) [1].

Classical clinical and histological parameters have been used to predict survival, development of metastatic disease

* Corresponding author at: Monter Cancer center, 450 Lakeville Road, Lake Success, NY 11042, United States. Tel.: +1 516 734 8900; fax: +1 516 734 8913.
E-mail address: DBudman@NSHS.edu (D.R. Budman).

1040-8428/$ – see front matter © 2007 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.critrevonc.2007.11.004

and/or direct therapy of breast cancer. These include the Nottingham Prognostic Index, Adjuvant! Online, and the St. Gallen criteria (Table 1) [2–5].

Consensus guidelines for adjuvant therapy are available from three groups: the National Comprehensive Cancer Network (NCCN), the International Consensus Panel on the Treatment of Primary Breast Cancer (the St Gallen group), and the European Society for Medical Oncology (ESMO) [4–6]. The recommendations of these groups, particularly with regard to the indications for adding chemotherapy to hormone therapy for women with low-risk, hormone responsive breast cancer, differ. The NCCN suggests the use of adjuvant chemotherapy in patients with a tumor size greater than 0.6 cm, moderately or poorly differentiated, or those with axillary nodal metastases, regardless of hormone receptor status [7].

Alternatively, international practice is often guided by recommendations from the International Consensus Panel, which suggests that hormonal therapy alone is sufficient adjuvant treatment for node-negative, estrogen receptor (ER)-positive tumors less than 2 cm, as long as they are well-differentiated, and have no evidence of peritumoral or vascular invasion [4,5]. However, approximately 25% of patients with node-negative breast cancer will die of their disease within 10 years without adjuvant systemic therapy [8]. Large clinical trials, such as National Surgical Adjuvant Breast and Bowel Project (NSABP) trials B-14 and B-20, have demonstrated the benefit of tamoxifen in conjunction with chemotherapy in women who have node-negative, estrogen-receptor-positive breast cancer [9–11]. A recent meta-analysis revealed that 6 months of an anthracycline-based poly-chemotherapy regimen reduced the relative annual breast cancer death rate by approximately 38% for women under 50 years of age, and 20% for women 50–69 years of age, irrespective of the use of tamoxifen and ER status, nodal status, or other tumoral characteristics [12].

A major dilemma facing oncologists arises with respect to treatment recommendations in the increasingly frequent, small, node-negative tumors discovered on screening breast imaging. Although early studies reported 10-year relapse-free survival rates greater than 90% in tumors less than 1 cm without systemic therapy, more recent data suggest inferior outcomes [13,14]. This recent overview suggests that patients with high-grade tumors and/or lymphovascular invasion have 10-year relapse-free survival rate of less than 75% in the absence of systemic therapy [13].

Over the past few years, basic research developments have led to a better understanding of the molecular biology and behavior of breast cancer. These data have led to the reality that breast cancer is a heterogeneous disease. Current therapies have been designed to take advantage of specific features of cancer cells. The International Breast Cancer Study Group (IBSG) was one of the first groups of investigators to analyze the concept of heterogeneity by evaluating the effects of adjuvant chemotherapy in different subgroups: estrogen receptor rich, ER-intermediate, and ER-low. There is now substantial evidence of a greater benefit with chemotherapy in ER-low or ER-negative disease [12,15–17].

However, since the likelihood of distant recurrence in node-negative patients treated with tamoxifen alone after surgical excision is approximately 15% at 10 years, at least 85% of patients may be over-treated with chemotherapy if it were offered to all patients [10]. The main limitation of chemotherapy and hormonal therapy is that the absolute gain in survival is small, even with patient selection by active schemes, such as Adjuvant! Online.

Decision making tools, such as Adjuvant! Online, do not consider predictive factors such as HER2 status or prognostic factors such as colloid or tubular histology; subsequently under-treatment and over-treatment of patients remain as potential problems. There is a critical need for a more precise identification and classification of breast cancer for

Table 1
Classical guides and criteria used to predict prognosis

	Patient characteristics	Predicted outcome
Adjuvant! Online	Age Tumor size LN Grade Hormone receptor status	Relapse rate/survival
Nottingham Prognostic Index	Tumor size LN Stage Histological grade	Survival
St. Gallen Criteria	Tumor size LN Grade Hormone receptor status HER2 status Menopausal status Peritumoral invasion	Relapse rate

LN: lymph node involvement.