ISSN: 2304-2354
Number 3, Volume 44, 2013

BREAST CANCER AND TARGETED THERAPY

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Abstract

Breast cancer is one of the best examples of cancer diseases in which the molecular genetic alteration determination has changed its treatment options. Breast carcinoma is a *heterogeneous disease* (molecularly and clinically) with different natural courses of the disease and different response to therapy. Routine *clinical care* deals with *heterogeneity* for *decision making* depending on clinical prognostic factors, predictive, mixed prognostic/predictive biomarkers and guidelines. The assessment of prognostic factors, meanwhile, in order to provide a prediction of outcome, has become an essential part of the histopathologist's role in the handling and histological reporting of breast carcinomas. Following international guidelines and producing evidence by them has moved toward improvement the treatment of this disease. It is our duty as professionals to bring those guidelines in practice and influence the medicine policy makers in their decisions for better distribution of health resources which is is very important for developing countries like Albania

Introduction

Pathologic features of breast carcinoma allow patients to be placed into low-risk or high-risk categories in terms of recurrence, free or overall survival. Those features include lymph node status, tumor size, tumor type, histologic grade, lymphatic-vascular invasion, tumor proliferation rate, and hormone receptor status [1]. Sentinel or axillary lymph node status and tumor size are well established prognosticators in breast carcinoma patients and are part of the staging criteria outlined by the UICCAJCC scheme [2]. Although it is not possible to cover all the prognosticators in detail, hormone receptor statud and status of Her-2 (c-erb-B2) are discussed here.

Molecular pathology and specific oncogene therapy

For a long time one of the main goals of oncology has been the creation of therapies directed only against specific tumor cells, while sparing action in other cells of the body, in contrast to the toxicity caused by conventional chemotherapy and conventional radiotherapy. This kind of therapy is called *monoclonal therapy*, and consists in developing monoclonal antibodies against tumour cells, and more specifically against receptors or growth factors in the neoplastic cells inhibiting thus proliferation of them [3]. Malignant cells are characterized by self-sufficiency to growth signals, insensitivity to anti-growth signals, limitless of replicative potential, sustained of angiogenesis, evading apoptosis, tissue invasion and metastasis. All this steps of carcinogenesis are steps in developing novel prognostic and predictive markers and also of developing targeted therapies. There are also being developed other types of therapies the principle of action of which lies in the discovery and recognition of mutations in the genome of neoplastic cells [4]. This is not only a new area in the treatment of the patients but also in the relationship between oncologist – pathologist, for the choose of the right diagnosis and most appropriate therapy for the patient. Breast cacer is a *heterogeneous disease* (molecularly and clinically) with different natural courses of the disease (**prognosis**) and different response to therapy (**prediction**). Routine *clinical care* deals with *heterogeneity* for *decision making* depending on clinical prognostic factors (TNM, stage, comorbidity,.....); predictive, mixed prognostic/ predictive biomarkers (ER, PR, HER2, grade....) and guidelines (NCI, NCCN, ...). The assessment of prognostic factors, meanwhile, in order to provide a prediction of outcome, has become an *essential part of the histopathologist's role* in the handling and histological reporting of breast carcinomas [5].

Proto-oncogene Expression

One of the most extensively studied proto-oncogenes in breast carcinoma is Her-2 (c-erb-B2) . The human epidermal receptor protein-2 (c-erbB-2; HER2) oncogene protein is a transmembrane