Tumori, 94: 370-383, 2008

Factors predictive of response to hormone therapy in breast cancer

Francesca Rastelli and Sergio Crispino

Istituto Toscano Tumori, Dipartimento Oncologico USL7, Siena, Italy

ABSTRACT

Aims and background. Approximately half of metastatic breast cancers expressing estrogen and/or progesterone receptors responds to endocrine therapy, and postoperative adjuvant endocrine therapy provides about a 50% reduction in the development of recurrent disease. A number of publications have focused on the correlation of biomarkers, in particular estrogen and progesterone receptors and HER-2/neu status as well as different gene profiles, multigene assays and genetic polymorphisms with response to hormone therapy. The purpose of this article is to review the literature to identify biological markers predictive of response to tamoxifen and aromatase inhibitors.

Methods. A computerized literature search through Medline and ASCO abstract databases was performed, applying the words "endocrine therapy" and "predictive markers" and each of the following: early and metastatic breast cancer, estrogen receptors, progesterone receptors, HER2/neu, multigene assays, polymorphisms. The last search was updated in June 2007. In the examined literature, biological markers were retrospectively assayed to establish whether such variables were predictive for endocrine therapy efficacy.

Results. The role of estrogen receptor content as a predictor of response to endocrine treatment was confirmed: benefit from endocrine treatment was directly proportional to estrogen receptor levels. Progesterone receptor status was only a strong time-dependent prognostic value, and it has not yet been validated as a predictive factor of tamoxifen efficacy. Retrospective clinical data from upfront and sequential studies of aromatase inhibitors were discordant regarding the degree of benefit of these drugs over tamoxifen according to progesterone receptor status. HER-2 positivity was associated with a significantly greater risk of endocrine therapy failure in metastatic and neoadjuvant settings. The current generation of genomic assays for tamoxifen sensitivity all contain a combination of prognostic information that it is difficult to integrate into clinical practice.

Conclusions. Available clinical data are inconclusive to support preferential use of aromatase inhibitors over tamoxifen in progesterone-receptor-negative and HER-2-positive tumors, but it was also clear that lower estrogen receptors, lower progesterone receptors, and positive HER-2 are associated with lower responsiveness to any type of endocrine therapy. Tumors overexpressing HER-2 are endocrine resistant and they require the blockage of the HER-2 pathway in addition to estrogen deprivation. Recent molecular studies have shown that endocrine responsiveness is to a large extent influenced by estrogen-receptor-related pathways. In the future, the key to the correct tailoring of hormone therapy will probably be the ability to subtype estrogen-receptor-positive breast cancer.

Key words: *aromatase inhibitors, breast cancer, c-ErbB2, estrogen-progesterone receptors, gene expression profile, tamoxifen.*

Correspondence to: Francesca Rastelli, c/o UO Oncologia, USL 7, Ospedale Alta Val D'Elsa, 53036 Campostaggia (Siena), Italy.
Tel +39-0577-994367/4429;
fax +39-0577-994366;
e-mail francesca.rastelli@libero.it

Received August 13, 2007;
accepted November 21, 2007.