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Response to CMF according to HER-2 overexpression

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Keywords

CMF, HER-2, node positive

Context

A major aim of current research in breast cancer is more effective targeting of chemotherapy. Biological markers may provide one way of identifying patients more or less likely to respond to a particular therapy/regimen. HER-2 overexpression appears to be a potential indicator of responsiveness to doxorubicin and paclitaxel, and conversely of unresponsiveness to tamoxifen. It has been suggested that HER-2 overexpression may result in a decrease in responsiveness to cyclophosphamide, methotrexate, and fluorouracil (CMF). This study examined HER-2 overexpression and clinical benefit in the 386 node-positive breast cancer patients in the first trial of CMF versus no treatment with a 20-year follow-up.

Significant findings

Overexpression was found to be inversely associated with oestrogen receptor (ER) and progesterone receptor (PgR) expression. Results showed a clinical benefit from CMF treatment irrespective of the HER-2 expression levels within the tumour. There was no evidence to suggest an inversion of treatment effect in patients with HER-2-overexpressing tumours. The authors concluded that patients with either HER-2-positive or HER-2-negative tumours obtained benefit from CMF treatment, and the poor prognosis associated with the HER-2 overexpression in the untreated group could be overcome by administration of CMF.

Comments

This is an interesting study indicating that, whilst there may be some evidence to suggest that either the anthracyclines or the taxanes may be the treatment of choice for patients with HER-2-overexpressing tumours, the classic CMF regimen still offers clinical benefit when compared to no treatment at all.

A major limitation of the study is its retrospective nature and the failure to access the tumour samples of all patients treated in the original trial. Nevertheless, the retrieval rate of 87% appears superior to that of previous studies in this area, which despite their deficiencies have had a major impact upon clinical decision making. This finding emphasises the importance of prospective studies in determining the true picture of HER-2 overexpression and its impact upon the efficacy of particular chemotherapy regimens.

Whether immunohistochemical techniques are the best way to determine HER-2 overexpression is also an issue of debate.

Methods

Randomised clinical trial, retrospective analysis, immunohistochemistry, Bayesian subset analysis

Additional information

Miles DW, Harris WH, Gillett CE, Smith P, Barnes DM: **Effect of c-erbB2 and oestrogen receptor status on survival of women with primary breast cancer treated with adjuvant cyclophosphamide/methotrexate/fluorouracil.** *Int J Cancer* 1999, **84**:354-359 ([PubMed%20abstract](#)).

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