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Comparison of different methods of HER-2 analysis in archival tissue

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Keywords

FISH, HER-2 gene amplification, HER-2 overexpression, immunohistochemistry

Context

Overexpression of the HER-2 oncogene is likely to be both a prognostic and a predictive factor in patients with breast cancer. There is considerable controversy over the best way to test for tumour HER-2 status. This study analysed HER-2 status in archival breast cancer tissue, by assessing the immunohistochemical (IHC) sensitivity of a series of antibodies. HER-2 status was also determined by fluorescence *in situ*hybridisation (FISH) of amplified genes.

Significant findings

The HER-2 gene was amplified in 28% of the tumours, whereas overexpression was seen in 26-42% of the tumours. Strongly positive IHC results (3+) with any of the antibodies were always associated with gene amplification whilst weakly positive results (2+) often were not. The authors concluded that tumours showing high levels (3+) of overexpression on IHC testing almost certainly have gene amplification, but that FISH testing should be considered for tumours with lower levels of positive expression.

Comments

This is a well designed and well performed study that again highlights the potential problems with the use of IHC in testing for HER-2 protein overexpression (see Additional information [1][2]). It makes the

interesting point that although the HercepTest has been approved by the US Food and Drug Administration for determining which patients should be offered anti-HER-2 therapy, the HercepTest was not in fact used to identify patients in the pivotal HerceptinR trials that led to the approval of its use. This paper emphasises the importance of the development of universal standardised techniques for HER-2 testing so that therapies can be targeted to patients with the highest chance of benefit.

Methods

Immunohistochemistry, FISH, paraffin sections

Additional information

1. Press MF, Hung G, Godolphin W, Slamon DJ: **Sensitivity of HER-2/neu antibodies in archival tissue samples: potential source of error in immunohistochemical studies of oncogene expression.** *Cancer Res* 1994, **54**:2771-2777 (PubMed abstract).

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1. Lebeau A, Deimling D, Kaltz C, Sendelhofert A, Iff A, Luthardt B, Untch M, Lohrs U: Her-2/*neu* analysis in archival tissue samples of human breast cancer: comparison of immunohistochemistry and fluorescence *in situ*hybridization. J Clin Oncol . 2001, 19: 354-363.