PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Her-2/neu expression in primary breast cancer and its lymph node metastases

ArticleInfo		
ArticleID	:	3782
ArticleDOI	:	10.1186/bcr-2001-68485
ArticleCitationID	:	68485
ArticleSequenceNumber	:	54
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2001–9–3 Received : 2001–9–13 Accepted : 2001–9–13 OnlineDate : 2001–9–13
ArticleCopyright	:	Biomed Central Ltd2001

ArticleGrants	:	
ArticleContext	:	1305833

Fatima Cardoso,[Aff1]

Aff1 Jules Bordet Institute, Brussels, Belgium

Keywords

Breast cancer, her-2, HerceptinR, primary metastases

Context

Trastuzumab (HerceptinR) is a recombinant monoclonal antibody that binds to the transmembrane growth factor receptor Her-2, and is one of the first successful examples of targeted therapy in the treatment of cancer. However, in about 60% of patients, who receive HerceptinR alone as first-line therapy, no objective responses are observed, even if the tumour has an intensive Her-2 positivity. The authors hypothesized that the high failure rate of treating patients with HerceptinR could result from different Her-2 expression between a primary tumour and its metastases. Since HerceptinR works by targeting the metastases, if at least some of the multiple metastases of a Her-2-positive primary breast cancer do not express Her-2, then HerceptinR would most likely not affect the course of the disease.

Significant findings

The authors analysed 196 lymph node-negative primary tumours, 196 lymph node-positive primary tumours, and three different lymph node metastases. For Her-2 positive primary tumours, 77% (95% confidence intervals [CI] = 59% to 90%) had entirely Her-2 positive metastases, 6.5% (95% CI = 8% to 21%) had entirely Her-2 negative metastases, and 16.3% (95% CI = 5% to 34%) had a mixture of Her-2 positive and Her-2 negative metastases. For Her-2 negative primary tumours, 95% (95% CI = 88% to 98%) had entirely Her-2 negative metastases. The authors conclude that this data suggest that differences in Her-2 expression between primary tumours and their lymph node metastases cannot explain the high fraction of nonresponders to HerceptinR.

Comments

These findings are consistent with other studies that compared the expression of Her-2 in primary tumour and its lymph node metastases. In a recently published article (see Additional information), where several biological markers were analysed, Her-2 presented the highest rate of concordance. Nevertheless, in both studies, a percentage of discordant cases, albeit small, exists. This study is of retrospective nature, and presents some surprising results which may be the result of technical limitations and/or selection bias: the rate of Her-2-amplified tumours (by FISH) among those with a immunohistochemistry score of 1+ (66%) or 2+ (97%) is much higher than usual. This emphasises the need for standardisation of methodology between different pathology laboratories. The high failure rate of HerceptinR in Her-2-positive patients cannot be entirely explained by discrepancies between primary and lymph node Her-2 expression. Of interest would be the comparison of Her-2 expression in the primary tumour and its distant metastases, since these are the main targets for metastatic breast cancer, and may be biologically different from regional metastases. Further studies aiming to identify the biological mechanisms of resistance to HerceptinR therapy are needed.

Methods

Tissue microarray, FISH, immunohistochemistry, Fisher's exact test

Additional information

Cardoso F, Di Leo A, Larsimont D, Gancberg D, Rouas G, Dolci S, Ferreira F, Paesmans M, Piccart M: **Evaluation of HER2, p53, bcl-2, topoisomerase II-a, heat shock proteins 27 and 70 in primary breast cancer and metastatic ipsilateral axillary lymph nodes.** *Ann Oncol* 2001, **12**:615-620 (PubMed abstract).

References

1. Simon R, Nocito A, Hubscher T, Bucher C, Torhorst J, Scraml P, Bubendorf L, Mihatsch MM, Moch H, Wilber K, Schotzau A, Kononen J, Sauter G: Patterns of Her-2/neu amplification and overexpression in primary and metastatic breast cancer. J Natl Cancer Inst. 2001, 93: 1141-1146.