Responsiveness of adjacent ductal carcinoma in situ and changes in HER2 status after neoadjuvant chemotherapy/trastuzumab treatment in early breast cancer-results from the GeparQuattro study (GBG 40)

Gunter Von Minckwitz, Silvia Darb-Esfahani, Sibylle Loibl, Jens Huober, Hans Tesch, Christine Solbach, Frank Holms, Holger Eidtmann, Klaus Dietrich, Marianne Just, Michael R Clemens, Claus Hanusch, Iris Schrader, Stephan Henschen, Gerald Hoffmann, Katharina Tiemann, Kurt Diebold, Michael Untch & Carsten Denkert

Adjacent ductal carcinoma in situ (DCIS) is found in approximately 45% of invasive ductal carcinomas (IDC) of the breast. Pure DCIS overexpresses HER2 in approximately 45%. There is uncertainty whether adjacent DCIS impacts on the response to neoadjuvant chemotherapy and trastuzumab as well as whether HER2 expression in IDC component or adjacent DCIS changes throughout treatment. Core biopsies and surgical tissue from participants of the GeparQuattro study with HER2-positive IDC were centrally examined for the area of invasive ductal component and adjacent DCIS before and after receiving neoadjuvant anthracycline-taxane-trastuzumab containing chemotherapy. HER2 overexpression in IDC and adjacent DCIS was quantified separately by immunohistochemistry using the Ventana(™) automated staining system. Pathological complete response (pCR) was defined as no residual invasive or non-invasive tumor tissue. Fifty-nine (37.3%) of 158 IDCs presented with adjacent DCIS at diagnosis. These tumors showed lower regression grades than pure IDC (P = 0.033). The presence of adjacent DCIS was an independent negative predictor of pCR [odds ratio 0.42 (95% CI 0.2-0.9), P = 0.027]. Adjacent DCIS area decreased from pre-treatment to surgery (r = 0.205) with 30 (50.8%) IDCs with adjacent DCIS showing complete eradication of adjacent DCIS. HER2 status of adjacent DCIS was highly correlated with HER2 status of IDC component before (r = 0.892) and after treatment (r = 0.676). Degree of HER2 overexpression of the IDC component decreased in 16 (33.3%) out of 49 patients without a pCR. These 16 IDCs showed lower RGs compared to the 33 IDCs with unchanged HER2 expression (P = 0.055). HER2-positive IDCs with adjacent DCIS is less responsive to neoadjuvant chemotherapy and trastuzumab compared to pure IDC. However, complete eradication of adjacent DCIS is frequently observed. HER2-overexpression of the invasive ductal component decreases in a subset of tumors, which showed less tumor regression.
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