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The hTERT blood plasma level is affected by the surgical removal of the tumor in early breast cancer patients

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Introduction: Breast cancer is a heterogeneous disease with different clinical courses. In order to better determine the prognosis and response to the therapy of breast cancer patients several different prognostic and predictive factors are in use today, but they all have limitations. One of potential new prognostic and/or predictive factors is the enzyme telomerase. The activation of the enzyme telomerase seems to be a crucial step in breast cancer progression. The telomerase consists of two functional components: the catalytic subunit of human telomerase reverse transcriptase (hTERT) and telomerase RNA template. The hTERT is multiplied in tumor samples of most human cancers. Furthermore, we were able to detect the hTERT in blood plasma of breast cancer patients.
Aim: The aim of our study was to determine, whether the presence of the hTERT in blood plasma of early breast cancer patients is affected by the surgical removal of the tumour.
Patients and Methods: Two blood samples were collected from all 93 patients. The first blood sample was collected prior the surgery on the day of operation and the second blood sample was collected one day after the surgery. The presence of the hTERT in the blood plasma was measured before and after the surgery in every patient. From all blood samples the hTERT mRNA was isolated, then the reverse transcription to cDNA was performed which was amplified by semi-nested PCR. The PCR products were separated by polyacrylamid gel electrophoresis.
Results: Before surgery hTERT mRNA was detected in 44/93 (47%) patients. After the surgery hTERT mRNA was detected in 26/44 (59%) patients and not detected in 18/44 (41%) patients. Additionally, after the surgery the hTERT was detected in 16/49 (33%) patients that were negative for the presence of the hTERT before surgery.
Conclusion: The presence of the hTERT in the blood plasma of early breast cancer patients is affected by the surgical removal of the tumor. The clinical significance of our findings is not yet known.

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An open-label study of neoadjuvant capecitabine (C) and docetaxel (D) with/without trastuzumab (T) to determine the role of p53 mutations in clinical and pathological responses in patients with recently diagnosed breast cancer (BC)

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Background: Cellular proliferation, survival, and genomic integrity are controlled by various processes, one of which involves the tumor suppressor gene p53. Disruption of the function of p53 leads to uncontrolled proliferation of damaged cells as a consequence of checkpoint defects, genomic instability, and inappropriate survival. Because of its relationship to patient outcome and survival, p53 mutation status is a potential prognostic indicator. However, immunohistochemical analysis cannot accurately identify p53 mutation status and cannot differentiate between the several functional defects that arise from mutations at specific sites of this multifunctional gene.
Materials and Methods: The primary objective was to define the rate of pathological complete response (pCR) plus near pCR in the affected breast after 4 cycles of neoadjuvant treatment with C+D±T in patients with HER2-neu negative (HER2−) or HER2-neu positive (HER2+) BC, respectively. Eligible patients had infiltrating HER2− or HER2+ stage II/III BC with no evidence of metastases and no prior systemic or local primary treatment. HER2+ patients also received weekly T. The study enrolled 140 (109 HER2−, 31 HER2+) patients. Prior to systemic therapy, breast tumor biopsy yielding 50–100 ng of genomic DNA was done. To analyze the p53 mutation status, the AmpliChip p53 test (Roche Diagnostics, in development), a DNA microarray-based sequencing method, was used. The AmpliChip p53 test is designed to detect all substitution single base changes and single base deletions in all coding regions of the p53 gene.
Results: A biopsy sample was obtained from 88 patients. A total of 47 p53 mutations were found in 44 (50%) patients. The mutations included 32 missense, 6 frameshift, 8 non-sense, and 1 splice site mutation. The mutations were widely distributed in exon 2, 4, 5, 6, 7, 8, 9, and 10. The p53 mutation status including the type and location will be analyzed in relation to the clinical and pathological responses. Updated data including clinical and pathological outcomes will be presented.
Conclusions: The AmpliChip p53 test is a rapid and standardized method to detect p53 mutations. The findings suggest that p53 mutations occur in at least 50% of patients with recently diagnosed infiltrating HER2− and HER2+ BC and are distributed in different functional domains of p53.

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Wide local excision with resection of cavity margins – Is it overkill or astuteness?

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Introduction: Residual disease at excision margins after breast conservation surgery influences local recurrence and therefore necessitates further surgical intervention. Although primary resection of cavity margins ensures completeness of tumour excision, it is associated with greater disfigurement. This study aims to evaluate the re-operation rate for margin positivity after wide local excision (WLE) with and without cavity margin resection.
Methods: Data were collected retrospectively from 01/06/01 to 31/04/06 on all patients undergoing WLE with or without cavity margin resection under the care of 2 consultant surgeons; one routinely performed cavity margin resection while the other did not. WLE was by mammographic needle localisation with post-excision mammographic confirmation of complete excision of specimen. Histological results were obtained for all patients and details on re-operations obtained.
Results: 598 patients (mean age-56 years; range 22−91) underwent WLE+/− axillary node sampling. Of these 68 patients had benign disease. 281/530 underwent WLE + cavity margins resection and 39 required a re-operation. 37/39 had only 1 re-operation while the remaining 2 had 2 re-operations. 13/39 had re-excision of cavity margins of which 10 had no residual disease. One patient had a mastectomy for a recurrence, one had a prophylactic mastectomy and 6 had axillary node sampling. 249/530 patients underwent WLE without cavity margin excision. 64/249 underwent re-operation of which 58 had 1 re-operation and 6 had 2 re-operations. 38/64 had re-excision of cavity margins of which 27 had no residual disease. Three had a mastectomy for tumour recurrence and 4 had axillary node sampling. The difference in the re-operation rate is significant with a chi-square of 7.923 using the Pearson's test with a p value of <0.01.
Conclusions: WLE combined with cavity margins resection is associated with a significantly lower rate of re-operation. Younger patients, axillary node positivity, tumour grade and multi-focal tumours are more likely to have margin involvement and therefore subsequent re-operation. Pre-operative anticipation of these factors combined with mammographic confirmation of completeness of excision should help the surgeon make an intra-operative decision for or against cavity margins resection. This can avoid undue removal of excessive normal tissue and subsequent disfigurement.

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Comparison of the cost-effectiveness of upfront letrozole or anastrozole, or switched exemestane versus tamoxifen for early breast cancer in hormone receptor positive (HR+) postmenopausal women: the UK perspective

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Background: Three randomized controlled trials have demonstrated that, in postmenopausal women with hormone receptor-positive (HR+) early breast cancer, upfront adjuvant therapy for 5 years with aromatase inhibitors (AIs) (BIG 1−98: letrozole [LET]; ATAC: anastrozole [ANA]) or switching to an AI after 2−3 years tamoxifen (TAM) (IES: 2−3 years exemestane [EXE]) is superior to 5 years TAM. This analysis evaluates the cost-effectiveness from a UK NHS perspective of 5 years LET, 5 years ANA, or 3 years EXE (after 2 years TAM) versus 5 years TAM using the same health economic model so that the cost-effectiveness of the three AIs can be compared
Methods: A Markov model was used to estimate the incremental cost per quality-adjusted life year (QALY) gained with the 4 therapy options in postmenopausal women with HR+ early-stage breast cancer. Probabilities of breast cancer events (contralateral; locoregional; soft tissue, bone, and visceral metastases) and adverse events (endometrial cancer, hip and other fractures, cardiovascular disease, thromboembolic events, and arthralgia) were based on the latest early breast cancer (Lancet) overview; published results of the BIG 1−98, ATAC, and IES trials; and UK population-based studies as appropriate. Conservatively, no carryover effect has been