detoxificate quinones and protect cells against neoplasia. NQO2, whose sequence is homology with NQO1, has a complicated and paradoxical function and remains a source of many questions. The real function of NQO2 on estrogen metabolites and its attribution to breast cancer susceptibility have not been evaluated yet.

Materials and Methods: In a hospital population-based case-control study of breast cancer, 888 cases and 695 age and menopausal status-matched controls were genotyped for the polymorphic NQO2. Six common single nucleotide polymorphisms (SNP) spanning this gene and one 29 base-pair insertion/deletion polymorphism (29bp-I/D) in promoter region, were chosen as tag-SNPs via Hapmap and dbSNP database and were genotyped. We investigated the association between variants in NQO2 and breast cancer susceptibility.

Results: A 29bp deletion polymorphism in the presumed NQO2 promoter region was associated with decreased breast cancer risk [odds ratio (OR) = 0.73, 95% confidence interval (95% CI): 0.61−0.88, P = 0.0007; permutated P = 0.007). Other two SNPs (rs2071002 and rs2070999) showed significant association with breast cancer susceptibility (P = 0.0051 and 0.0152; permutated P = 0.034 and 0.096 respectively). After being adjusted by epidemiological and clinical factors such as age, age at menarche, menopausal status, BMI and parity, DD genotype of 29bp-I/D had a OR of 0.47 (95% CI: 0.26−0.85); GG genotype of rs2071002 had a OR of 0.66 (95% CI: 0.45−0.97), both displaying protective effects against breast cancer. Another common haplotype in the block consisting of 3 SNPs was significantly associated with breast cancer (P = 0.03).

Conclusions: The observed multiple breast cancer-associated genetic variants suggested that the NQO2 gene plays an important role in breast carcinogenesis. Further analysis of the molecular mechanism is needed to be conducted.

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Prospective registration in the Leiden region facilitates exchange of good clinical practice between multidisciplinary mamma teams

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Background: Quality of general health care and specifically breast cancer care is a hot topic nowadays. It is questionable whether all in hospital quality measurements are sufficiently reliable, representative and reproducible. Therefore, we started a prospective breast cancer and DCIS data registration study concerning diagnosis and treatment.

Methods: In 2005, all 9 hospitals in the CCCW region committed themselves into this project. Registration started in 01−01–2006. During 2007, data were collected for all patients diagnosed with either breast cancer or DCIS in 2006. Registration was carried out by co-workers of the National Cancer Registry. Data were derived directly from the hospital patient files, including the pathology reports, nine months after the incidence date. Results are given as means for each hospital and are compared with the mean results of the 9 hospitals together.

Results: In 2006, 1,363 breast cancer patients were included, 1,237 patients underwent surgery. Breast conserving therapy varied between 47−61% in the 9 hospitals. In 68−98% axillary nodes were identified after sentinel node procedure. Radiotherapy as part of breast conserving therapy occurred in 92–100%. Tumour free resection margins of the first lumpectomy varied between 61−85% in the 9 hospitals. In patients under 70 years with more than 4 positive axillary nodes, locoregional radiotherapy after modified radical mastectomy was given in 67–100%. Of the patients with tumors larger than 3 cm or axillary node metastases, and younger than 50 years, 85–100% received adjuvant chemotherapy, whereas 75–100% of the patients younger than 70 years with negative ER, PR receptors received adjuvant chemotherapy. Radiotherapy was started within 4 weeks after surgery in 0−28% and adjuvant chemotherapy in 9−60%. Patients (<50 years) with endocrine sensitive tumours (>3 cm or with axillary node metastases) 63–100% received adjuvant hormonal therapy. When overexpression of HER 2 was present adjuvant trastuzumab treatment (if indicated) was given in 50–100%.

Conclusion: Our prospective registration project appeared feasible, differences between hospitals were noted and indicate the usefulness of monitoring daily clinical practice in our region. Based on these objective data, improvements in breast cancer care can be initiated.

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Positive bone marrow biopsy is associated with a decreased event-free survival in patients with breast cancer

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Background: Bone marrow (BM) biopsy has been suggested as an independent prognostic tool to improve staging in patients with breast cancer.

Materials and Methods: 246 consecutive patients operated for breast cancer from June 2000 to June 2007 who signed an informed consent were enrolled in this protocol. Data were collected prospectively in to a computerized database. Patients underwent SLN biopsy, and lymph nodes were analysed with serial sections and stained with hematossilin-eosin and immunohistochemestry. At the end of procedure a BM aspirate from the iliac crest was obtained and 5−10 cc of blood collected, and since 2002 a peripheral blood (PB)sample was also obtained. Both CEA and Mammoglobin specific nested reverse transcriptase (RT) polymerase chain reaction (PCR) assays were used to examine BM and PB samples.Results were blinded to patients and clinicians.

Results: The median age was 56 years (range 34−80), and the median tumor diameter was 1.5 cm (range 0.2−4.5). BM aspirates were unsuccessfull in nine patients, and RT-PCR was not technically feasible in additional 15 women, leaving 222 patients available for analysis of results and follow-up.104/222 patients (47%) had either a BM or a PB test positive. Concordance between BM and PB, and between CEA and Mammoglobin samples was 84% and 79% respectively. Discordance between nodal and BM status (N−/M+ or N+/M−) was verified in 87/222 cases (39%). Nodal status was correlated with a positive test (37% vs 58%, p = 0.001), while tumor diameter, grade and hormonal status were not. At a median follow-up of 50 months event-free survival was significantly lower in the BM+ group (84% vs 96%, p = 0.004).Event-free survival for N−/M− patients was 96%, for N+/M+ patients was 75%, while patients with only one status positive (N−/M− or N+/M−) had an intermediate survival (88%) (p = 0.001).

Conclusions: This study confirms that BM biopsy has an impact on event-free survival of patients with operable breast cancer. This may identify a substantial subgroup of patients N−/BM+ with a decreased survival who may need a more aggressive approach.

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Economic evaluation of zoledronic acid for the prevention of osteoporotic fractures in post-menopausal women with early-stage breast cancer receiving aromatase inhibitors in the United Kingdom

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Background: Aromatase inhibitors (AIs) are used as adjuvant therapy in early-stage breast cancer (BCa). AIs are associated with accelerated bone loss in a population already at higher risk for osteoporosis and fractures. The Z-FAST trial demonstrated that zoledronic acid (ZOL) prevents AI-associated bone loss (AIBL) in postmenopausal women (PMW) with BCa. Information on the economic consequences of using ZOL in this context is limited. The present analysis assessed, from the UK's National Health Service perspective, the cost-effectiveness of ZOL in the prevention of fractures in PMW with AI treated BCa.

Methods: A Markov model was developed to project the lifetime incidence of osteoporotic fractures as a function of bone mineral density (BMD) for women with early-stage breast cancer (aged 60 years old at therapy initiation). In the model, patients were assumed to receive AIs for 5 years with ZOL (4 mg IV infusion q 6 months), either administered upfront to all patients (upfront arm) or as salvage therapy only in patients with AIBL (delayed arm). The model also simulated separately the outcomes of patients receiving no ZOL therapy. Subsequently the model simulated the impact of fractures on costs, quality of life and mortality. Uncertainty was addressed via multivariate probabilistic sensitivity analyses (PSA), which involved 1,000 model simulations using input values drawn from probability distributions. All future costs and effects were discounted at 3.5% per annum.

Results: Upfront ZOL treatment resulted in a gain of 0.052 QALY (95% CI: 0.027−0.077) v. delayed ZOL treatment. Upfront therapy resulted in an incremental cost of £25,515 per QALY gained. In the PSA, the cost per QALY was less than £38,730 in 95% of the 1,000 model replicates. When compared to no treatment, upfront ZOL therapy was associated with a gain of 0.080 QALY (95% CI: 0.041−0.118), with an incremental cost of £21,821 per QALY gained. In this case, the cost per QALY was less than