studies are needed to better codify the therapeutic sequence in order to spare patients from unnecessary secondary effects and iatrogenic complications.

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Breast cancer during pregnancy – a prospective and retrospective European registry (GBG-20/BIG02−03)

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Background: In the treatment of the pregnant breast cancer patients, the evidence upon which we base our decisions has been largely limited to case reports, case-control studies and retrospective cohorts. Therefore, the German Breast Group has launched a registry (GBG-29/BIG 02−03) for patients with breast cancer that has been diagnosed during pregnancy.

Material: Every pregnant breast cancer patient is eligible. The primary endpoint is the fetal outcome 4 weeks after delivery. Secondary endpoints are maternal outcome of pregnancy, stage and biological characteristics of breast cancer, breast cancer therapy (treatment, response to chemotherapy, type of surgery), sensitivity and specificity of diagnostic procedures, outcome of the newborn after 5 years, outcome of breast cancer 5 years after diagnosis.

Results: From April 2003-December 2007, 122 patients have been prospectively (n = 39) and retrospectively (n = 83) registered. The median age is 33 years (range 24−43). T1−2: 71.7%; T3−4: 28.3%; N+ 66.6%; ductal invasive 83.8%, lobular 4.8%, inflammatory 4.8%, Grading 3: 69.5%, ER/PR neg 53.5%; Her-2 pos: 41.3%. At the time of diagnosis the median gestational age is 21 weeks; 21.6% of all patients have been diagnosed during the 1st, 43.3% during the 2nd and 35.1% during the 3rd trimester. From the patients who continued pregnancy, 33.3% received surgery only, 43.2% were treated by surgery and chemotherapy, 5.4% were treated only by chemotherapy and 2.7% had no treatment. Cytotoxic regimens used during pregnancy: EC/AC n = 23, CMF n = 11, FEC = 7, taxane = 11. The median time of delivery was 36 weeks (range 30−42), 54 newborns exposed to systemic therapy had alopecia (1), small for gestational age (1), 1 had trisomia 18 and died one week after birth, 1 had necrotic enterocolitis and died 3 weeks after birth. Fetal outcome in babies, who received intrauterine chemotherapy was not different from those who did not.

Conclusion: Pregnant breast cancer patients can probably be treated as close as possible to standard recommendations in specialized multidisciplinary teams. The registry needs to be continued to get better data on long time follow-up.

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Febrile neutropenia, related hospitalizations and chemotherapy delivery in breast cancer patients younger than 65 years receiving pegfilgrastim primary prophylaxis vs current practice neutropenia management

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Background: Elderly patients are recognized as being at substantial risk of febrile neutropenia (FN) during cancer chemotherapy (CT), but younger patients are also at risk, particularly with the trend toward more intense regimens. Furthermore, FN frequently leads to CT dose modification. Delivery of planned dose is essential in younger patients who are likely to be treated with curative intent. In this subgroup analysis from the NeuCuP project, we compare the relative merits of FN prevention with pegfilgrastim primary prophylaxis (PPP) vs current practice neutropenia management (CP) in patients <65 years of age.

Methods: Studies involving breast cancer CT regimens with moderately-high (15−20%)/high (⩾20%) risk of FN were identified by literature review. For this integrated analysis, individual patient data were available from 8 clinical trial and 3 observational studies involving these regimens and PPP (pegfilgrastim 6 mg in all cycles) or CP neutropenia management (no granulocyte colony-stimulating factor [G-CSF] or pegfilgrastim/daily G-CSF in any cycle). Descriptive data are reported for the subgroup of patients aged <65 years with respect to FN over all cycles (primary outcome measure) and other related parameters.

Results: 2024/2282 patients were aged <65 years (1149 PPP, 875 CP). Patients' mean age (±SD, years) was 49.0±8.5 for PPP vs 50.1±8.6 for CP, around one quarter had Stage IV disease (27% vs 28%) and about one third had prior CT/radiotherapy (30% vs 37%). The most common CT regimens were docetaxel (Doc), Doc/doxorubicin (A)/cyclophosphamide (C), ADoc and AC → Doc. In cycle 1, 76% of CP patients received no G-CSF, 12% received pegfilgrastim only, and 12% received various G-CSF regimens. FN, FN-related hospitalization and CT delivery parameters for PPP vs CP are shown (Table).

	All cycles n (%) [95% CI]		Cycle 1, n (%) [95% CI]	
	PPP (N = 1149)	CP (N = 875)	PPP (N = 1149)	CP (N = 875)
FN	60(5) [4, 7]	136(16) [13, 18]	34(3) [2, 4]	80(9) [7, 11]
FN-related hospitalization	39(3) [2, 4]	82(9) [7, 11]	29(3) [2, 3]	50(6) [4, 7]
Dose delay >3 days	173(15) [13, 17]	137(16) [13, 18]	N/A	N/A
Dose reduction ⩾15%	93(8) [7,10]	204(23) [21,26]	N/A	N/A

Conclusions: FN and related hospitalizations were less frequent in younger breast cancer patients who received PPP rather than CP neutropenia management in support of CT with moderately-high/high FN risk. Fewer CT dose reductions occurred in the PPP group. PPP may offer better FN protection and aid delivery of planned CT doses in this patient group.

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Breast units in Germany – yes or no

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Background: Currently there is an ongoing discussion concerning the necessity of certified Breast Units (CBU) in Germany. The establishment of new BU leads inevitably to a decreased density of Breast Cancer (BC) treating hospitals. On the other hand better treatment options are being hoped for BC patients treated at BU. For that reason we analyzed the treatment of BC in CBU in comparison to not certified hospitals regarding treatment strategies, local recurrence (LR), overall survival (OAS) and the impact of continual education in northern Germany.

Material and Method: A retrospective analysis of 1327 patients diagnosed with BC in the years 1997/98 and 2005/06 was performed. Data has been collected from the Cancer Register Rostock using the "Giessener Tumor Documentation System" (GTDS©). BC patients who received treatment either at a CBU or a not-certified hospital with the following criteria were included: pT1−4, pN0/+, cM0/+. Pearson's chi-square test and survival analysis using Kaplan Meier were performed for statistical analysis.

Results: OAS ($p = 0.398$) and LR ($p = 0.398$) did not differ with regard to the treating hospital. Concerning the applied surgical methods (breast conserving therapy, oncoplastic surgery, modified radical mastectomy) a significant difference ($p < 0.001$) was found between patients being treated at a CBU or a not certified hospital. The rate of breast conserving surgeries was significant higher in CBU and additionally the rate of secondary operations was fewer. The number of BC treating hospitals decreased from 1997/98 to 2005/06 from 7 to 3. Simultaneously the number of patients treated at certified BU increased.

Conclusion: Despite missing advantage for OAS, the treatment of BC patients should be performed at CBU. With increased numbers of patients the surgical treatment was superior in CBU and with more treatment options the patient satisfaction and quality of life was increased.

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Common polymorphisms and haplotypes in NAD(P)H:Quinone Oxidoreductase-2 (NQO2) make a contribution to breast cancer susceptibility

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Background: Clinical evidence supports a role of estrogen in breast carcinogenesis. The estrogen metabolites such as semiquinone and quinone can lead to depurination and mutation of DNA. Although it has been elucidated that NAD(P)H:quinone oxidoreductase-1 (NQO1) can

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