Patients and Methods: Data on 57 PABC patients who received neoadjuvant chemotherapy (NACT) were collected. To evaluate the theoretical response rate to chemotherapy, we used well-calibrated logistic regression-based nomograms that have been previously developed to calculate individual probability of pathologic complete response (pCR) according to the chemotherapy regimen given. Theoretical and observed pCR rates were analyzed in terms of discrimination and calibration.

Results: Observed rates of pCR were concordant with predictions in the whole population and in the subgroups that were analyzed. For the whole population, the area under (AUC) the receiver-operated curve (ROC) was 0.77 (95% CI, 0.66–0.87). The calibration of predicted and observed probabilities was excellent, with no statistical difference (P = 0.77). In the subgroup analysis (NACT initiated during pregnancy or postpartum, NACT with only anthracycline or both anthracycline and taxanes), discriminations assessed by AUC were significantly above 0.5, except for patients treated with anthracycline-only NACT. The calibration curves were satisfactory but chemosensitivity was poorer in the anthracycline-only subgroup.

Conclusion: Through the use of nomograms, our study demonstrates that PABC is as chemosensitive as classic breast cancer and suggests that taxanes should be part of the NACT regimen for PABC.

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Zoledronic acid (ZOL) as add-on therapy in patients with tumour residuals after neoadjuvant chemotherapy for primary breast cancer − first interim safety analysis of the NATAN study (GBG 36)

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Background: Patients (P) with residual disease after neoadjuvant chemotherapy (NACT) are considered to be chemo-resistant. There is growing evidence, that ZOL has beneficial effects in the metastatic and adjuvant treatment.

Patients and Methods: P who had invasive tumor residuals after a minimum of 4 cycles of an anthracycline/taxane containing NACT were eligible. P were randomized to receive ZOL 4 mg i.v. vs. observation. ZOL was given for the first 6 months (mos) q 4 wks, q 3 mos the following 2 yrs, and q 6 mos for the last 2.5 yrs. Postmenopausal P with hormone receptor (HR)-pos BC received letrozole, premenopausal P received tamoxifen. HER2-pos P received trastuzumab since an amendment in 2007.

Primary objective is the event-free survival after 5 yrs of ZOL vs. observation. The total number of P required for the trial is equal to 654 to observe 316 events after the end of follow up.

As the safety of long term use of ZOL in this population is not fully characterized, a pre-planned interim safety analysis was performed after the first 100 P received ZOL for 2 yrs.

Results: Between 2/2005 and 5/2009 693 P were enrolled. Time between surgery and randomization was <4 mos in 48.4%, 4−12 mos in 34.5%, and 13−36 mos in 17.1% of P. The median age was 50.9 yrs (range 33.7–88.2), 72.3% of P were postmenopausal. 82% had HR-pos and 19% HER2-pos BC.

99 of 100 P started ZOL therapy. After a 2 yrs interval, 75 P (75%) were still under treatment, 70 received the full dose and 5 stopped therapy due to relapse. 24 P (24%) discontinued the study early due to toxicity (3), withdrawal of consent (5), patient's wish (7), death (1, not related to medication) and administrative reasons (8). During the first 2 yrs, a total of 23 AEs were reported due to joint pain (39%), headache (17%), vertigo & chills (each 13%), hot flushes (9%), hypocalcaemia & circulation problems (each 4%). Treatment delays occurred in 50% (median 6 d, range: 1 to >50 d).

Conclusion: This is the first post-neoadjuvant phase III study. No unexpected AEs and no osteonecrosis of the jaw were reported, demonstrating that long term ZOL is feasible in this setting. The first interim efficacy analysis is expected in 2011.

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Influence of pathologic tumour characteristics on ipsilateral breast tumour recurrences after breast conservation and neoadjuvant chemotherapy

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Background: It has been reported that breast conservation after neadjuvant chemotherapy (NAC) could be asociated with an increase in Ipsilateral Breast Tumor Recurrences (IBTR) rates. The purpose of this study is to determine incidence and prognostic factors of IBTR in patients with breast conservation after NAC.

Materials and Methods: Using our breast cancer (BC) data base we identified 173 women treated with NAC followed by lumpectomy between 1998 and 2009. Clinical stage (TNM) at diagnosis was stage I in 1.2%, stage IIa in 49.4%, stage IIb in 32.6% and stage III in 16.8%. NAC was based on anthracyclines plus taxanes in 67.4% of cases. All patients had negative resection margins (24.6% required rexcision by second surgery). All patients were treated with adjuvant external-beam radiation therapy to the affected breast, (median delivered dose 50 Gy) followed by boost to tumor bed with external radiotherapy in 33% or interstitial brachytherapy in 53.8% of cases. Internal mamary or supraclavicular node radiation was administered in 8.1% and 44.8% of patients respectevely.

Results: At a median follow up of 50 months, 7 patients (4%) developed IBTR. Actuarial IBTR free was 96.7% (±3%) at 4 year. Variables asociated with increased IBTR were: ER negative vs ER positive (4 year IBTR free 92% vs 100%, p = 0.02), HER2 positive vs HER2 negative (4 year IBTR free 87% vs 100%, p = 0.001), pCR vs no pCR (4 year IBTR free 93% vs 100%, p = 0.02), Multifocal pattern of residual disease vs sollitary mass (4 year IBTR free 93% vs 98%, p = 0.06). Others analyzed variables that didn't show association with IBTR were residual tumor size, DCIS in specimen, lymphovascular space invasion, clincal stage at diagnosis and margin status negative at first surgery. In multivariate analysis only HER2 positive disease was associated significatively with increased IBTR (HR: 12.2 95% IC 1.3–110, p = 0.026). Five out of seven patients that experienced IBTR were HER2 positive, all of them had been treated with trastuzumab and their median time to relapse was 30 months.

Conclusions: After NAC, breast conservative surgery with negative margins followed by radiotherapy results in very low rates of IBTR. However, lumpectomy should be carefully considered in patients with HER2 positive tumor, specially pCR is not achieved after NAC.

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Breast conserving therapy after neoadjuvant treatment: Is it oncologic safe?

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Objective: Several prospective trials report about a potentially increased risk of local recurrence free survival (LRFS) after breast conserving treatment (BCT) following neoadjuvant chemotherapy. The aim of this study was to investigate this issue at a large single cancer centre series with well documented neoadjuvant therapy and follow-up.

Method: All consecutive patients undergoing breast cancer surgery after neoadjuvant chemotherapy (3xCMF or4−6x EC) between 1995 and 2007 were included. Subjects were separated into three groups, group 1 was scheduled for mastectomy and eventually was mastectomized (MX-MX), group 2 was scheduled for mastectomy but received BCT (MX-BCT) and group 3 was scheduled for BCT before and received BCT after neoadjuvant treatment (BCT-BCT). Indications for mastectomy were no change or progressive disease, inflammatory breast cancer and multicentricity as well as R1 resection after several attempts of breast conservation.

Results: 308 patients were included in the analysis. The median follow up were 60 months. Overall and distant recurrence free survival (OS and DRFS) was worse (both p = 0.001) in MX-MX patients (OS: 76%; DRFS: 58%) compared with MX-BCT (OS:91%; DRFS: 78%) and BCT-BCT patients (OS: 95%; DRFS: 87%). There was only a non-significant trend for an increased LRFS in downsized patients (MX-BCT=87%; BCT-BCT=96%; MX-MX=91%; p = 0.07). This difference was mainly due to the comparison