(median 8, range 1−8). All 8 cycles were completed by 72.4% of pts (15 pts were still on treatment). Median relative dose-intensity of C was 89.9%. The most common grade 3/4 clinical AEs related to C were: hand-foot syndrome (Grade 3 18.6%), diarrhoea (3.5%), fatigue (2.8%), irregular menses (2.4%), neutropenia (1.9%), nausea (0.9%), vomiting (0.7%), bilirubin elevation (0.7%), sensory neuropathy (0.7%) and nail changes (0.5%).

Conclusions: The safety profile of adjuvant C as maintenance therapy is consistent with its known toxicity profile. This analysis will be updated at the meeting with safety data from all randomised pts (876).

	Arm A, C (n = 435)	Arm B, Observation (n = 418)
Median age, years	50	49
KPS, %		
80	1.8	4.1
90	12.9	15.8
100	85.3	80.1
Node-positive (post-surgery), %	45.2	43.0
Basal phenotype, %	72.0	72.7
Histology, %		
ductal	88.1	86.8
lobular	1.8	2.2
other	10.1	11.0
Median tumor size, cm (range)	2.7 (0.8–11.0)	2.7 (0.5–14.0)
Post-menopausal, %	70.1	67.0
Prior standard chemotherapy, %		
Anthracyclines without taxanes	32.1	31.8
Anthracyclines and taxanes	67.9	68.2

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Can Surgery Be Avoided in Patients with Breast Cancer Who Achieve a Complete Clinical Response to Neoadjuvant Chemotherapy?

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Background: The objective of this study was to evaluate the local recurrence rates in patients with primary breast cancer who achieved a complete clinical response (cCR) to neoadjuvant chemotherapy and did not have surgery.

Materials and Methods: 148 women who achieved a cCR to neoadjuvant chemotherapy were identified from a prospectively maintained database (1995–2011) of 667 patients. 122 patients went on to have surgery (either wide local excision or mastectomy) followed by radiotherapy. 26 patients (median age 49, range 35−72 years; T2-T4, N0-N3, M0) did not undergo surgery but instead received radical external beam radiotherapy. Surgery was avoided due to either physician or patient choice. Recurrence was defined as first relapse of disease, either local (ipsilateral breast and/or axilla) or distant.

Results: All 26 patients who did not have surgery received neoadjuvant chemotherapy with 20 patients (77%) receiving anthracycline-based (FEC, FAC, ECF), 5 (19%) MMM and 1 (4%) CMF chemotherapy. The median number of cycles was 6 (range 4−8). Chemotherapy was followed by radical external beam radiotherapy to the breast +/− supraclavicular fossa and axilla (median dose delivered, 60 Gy in 2 Gy fractions). All were identified as operable at diagnosis including 3 patients who had supraclavicular lymphadenopathy. All 26 patients achieved a final cCR in the breast to chemotherapy. 21 patients had imaging with mammography and/or ultrasonography to assess radiological response at the end of neoadjuvant chemotherapy, of which 19 had a complete response and 2, a partial response. After a median follow-up of 144 months, 10/26 (39%) patients experienced local disease recurrence (2 also had distant recurrence) and 4/26 (15%) patients with distant metastases only. Patients with local recurrence only, went on to have a mastectomy whilst those with distant disease received systemic therapy. There were 10 deaths, 9 of which were breast cancer related (35%).

Conclusions: In patients achieving a cCR following neoadjuvant chemotherapy and who avoided surgery, local recurrence rates were high. As a result, practice in our institution has changed to include insertion of clips and surgical excision on completion of chemotherapy. With increasing pathological complete response rates to more active chemotherapy schedules (including taxanes +/− trastuzumab), it has been proposed that surgery could potentially be avoided in certain patients. However, our results demonstrate that caution should be exercised.

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The Role of Cyclin D1 in Planning of Endocrine Therapy for Women of Postmenopausal Age with Breast Cancer

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Background: Nowadays tamoxifen still remains the primary drug in breast cancer endocrine therapy. However, its application is limited due to the resistance of tumor cells. The search of adequate biomarkers is one of the most actual problems in prognosis of effectiveness of tamoxifen adjuvant therapy. The most perspective biomarker is cell cycle regulator cyclin D1. The objective of our work was to evaluate the effectiveness of tamoxifen in adjuvant therapy of hormone-receptor-positive breast cancer in women of postmenopausal age with cyclin D1 expression and to compare the effectiveness of tamoxifen and anastrosole in adjuvant therapy of hormone-receptor-positive breast cancer in women with cyclin D1 expression more than 30%.

Material and Methods: To evaluate the effectiveness of tamoxifen we have researched 2 retrospective groups of 70 patients with hormone-receptor-positive T1−4N0−3M0 breast cancer that have been on regular medical check-up for a period of 5 years or that had previously undergone treatment. On the basis of the archive histological material we have revealed cyclin D1 in tumor cells. To compare the effectiveness of tamoxifen and anastrosole we have additionally researched 1 additional group of 50 patients with breast cancer and cyclin D1 expression more than 30% that have been on regular anastrozole treatment for a period of 27 months.

Results: Patients with lack of cyclin D1 expression or with low quantitative value (according to our data less than 30%) have no neoplastic process progression throughout the 5 years of tamoxifen adjuvant therapy. On the contrary, women with moderate and high cyclin D1 expression (more than 30%) had a relapse of tumor. Thus, distant metastasis is prognosed in 5 years of observation in this patient's group. Moderate level of cyclin D1 expression was observed in 45 (64%) patients and 28 (62%) of them had progression with metastasis in bones, 9 (20%) metastasis in soft tissues, 2 (4%) metastasis in lungs and 6 (14%) relapse in postoperative scar. High expression was revealed in 25 (35%) women and 17 (68%) of them had bone affection, 7 (28%) soft tissue metastasis and 2 (4%) tumor relapse in postoperative scar. The average period of tumor relapse and progression of neoplastic process in patients with cyclin D1-positive breast cancer is 20 months. Patients who have cyclnin expression more than 30% and receive anastrosole in adjuvant have no tumor relapse and progression throuhgh out 27 months of observation.

Conclusion: Women with hormone-receptor-positive cyclin D1-negative breast cancer on early stages have more prolonged non-relapse period during the tamoxifen adjuvant therapy. Patients with cyclin D1-positive breast cancer are less sensitive to tamoxifen treatment and in adjuvant regime should receive therapy with other effective equivalent drugs (aromatase inhibitors). It is necessary to continue the research of cyclin D1 as biomarker that could influence on the choice of treatment between tamoxifen and aromatase inhibitors.

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Prognostic Factors for Triple Negative Breast Cancer Patients with Preoperative Systemic Chemotherapy

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Background: Triple negative breast cancer (TNBC), which is immunohistochemically characterized by lack of expression of the estrogen receptor (ER), progesterone receptor (PgR), and HER2, tends to show visceral metastasis and aggressive clinical behavior. The aim of this study is to identify the prognostic factors for patients with TNBC after receiving preoperative systemic chemotherapy (PST).

Materials and Methods: Among 4195 operable primary breast cancer patients, 135 TNBC patients who underwent preoperative systemic therapy between 2000 and 2009 were investigated. The significant prognostic factors among clinicopathological characteristics including familial history, menopausal status, body mass index (BMI), UICC staging before PST, chemotherapy regimen, completion of scheduled chemotherapy, clinical response, surgical procedure, radiotherapy, histological grades, pathological invasive size, pathological nodal status, lymphatic invasion, vascular invasion, HER2 status (0 or 1), pathological complete remission,

were demonstrated by Kaplan-Meier analysis and Cox proportional hazard model for disease free survival (DFS) and overall survival (OS).

Results: Among the 135 TNBC patients, median age was 54 years old, median tumor diameter on palpation was 4.5 cm (Min-Max; 1−15 cm), and there were 2 UICC stage I, 50 stage IIA, 40 stage IIB, 21 stage IIIA, 20 stage IIIB, and 2 stage IIIC patients. Seventeen out of 135 patients had family history of breast cancer within second-degree relatives. Body mass index of the 135 patients were classified into 97 normal (18.5−25), 10 underweight (<18.5), 28 overweight and obese (>25) patients. One hundred twenty three patients underwent both anthracycline and taxane containing regimen, 5 patients had anthracycline only, and 7 patients had taxane only. It was demonstrated that clinical response rate was 76% including 44 patients (32%) of clinical complete response (CR) and 59 patients (44%) of partial response (PR) and pCR was observed in 24 (18%) patients. Median disease free survival (DFS) was 44.4 months and median overall survival (OS) was 49.2 months. Univariate analysis showed that completion of chemotherapy, good clinical response, low histological grade, small pathological invasive size (pT), less positive node, no lymphatic invasion (ly−), no vascular invasion (v−), and pCR were the significant factors for both favorable DFS and OS. Multivariate analysis demonstrated that completion of chemotherapy, good clinical response, low histological grade, less positive nodes, and v− were the significant factors for favorable DFS and OS. The pCR was not a significant prognostic factor for TNBC patients receiving PST.

Conclusions: Our data demonstrated that pCR was not independent favorable prognostic factor among TNBC patients receiving PST. Clinical response, histological grades, nodal status, and vascular invasion, instead of pCR, were significant factors for the patients' prognosis.

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Neoadjuvant Endocrine Therapy: Retrospective Analysis of Some Mechanisms of Resistance

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Background: At least three randomized trials of neoadjuvant endocrine therapy were conducted in our cancer centers and published (Semiglazov et al. Proc. Am Soc. Clin. Oncol. 2004; 22(145): 519: J Clin. Oncol 2005: 23; 530; Cancer 2007: 110; 244–254).

Patients and Methods: A total of 440 postmenopausal women with ER-positive and/or PgR-positive breast cancer (T2N1−2, T3N0−1, T4N0M0), previously (2001–2007) received neoadjuvant endocrine therapy of aromatase inhibitors [IA] (anastrazole, letrozole, exemestane; n = 211) or tamoxifen (TAM) [n = 229], were included into retrospective analysis.

On the basis of immynohistochemical (IHC) analysis of the archive pathological material we reevaluated the levels of expression of ER/PgR, HER2 and cyclin D1 expression (Histocore-Labvision) before neoadjuvant therapy (cut biopsy material) and after surgery (surgical specimens).

Results: There was a higher overall rates of clinical objective response (ORR) among patients of both arm with high levels of ER (Allred score $\geqslant$ 6) [ORR = 53% in TAM group vs 70% in AI group].

Co-expression of hormone receptors (HR) and HER2 was revealed in 17% of 440 patients. Our data confirm previously results (Ellis et al, 2001) that TAM is less effective than AI in HER2 + and HR+ tumors (ORR=23% in TAM arm vs 47.7% in AI arm; p = 0.052).

Over-expression of cyclin D1 has been linked to breast cancer growth, as well as development of resistance to hormone therapy.

Cyclin D1 low level (less than 30%) was revealed in 79 of 142 patients (55.6%), moderate level (>30−70%) in 53 patient (37.3%), high level (>70%) in 26 patient (18.3%). More than 60% patient with low level of cyclin D1 expression responded to endocrine therapy (ORR = 65% in TAM group vs 76% in A1 group, p = 0.072). There was clinical response with AI (ORR = 46.6%) but not with TAM in patient whose tumor expresse high level cyclin D1. Striking down regulation in cyclin D1 and PgR were seen only in the AI arm.

After a mean follow up 60 months distant recurrences were observed in 25.5% of patients in TAM arm vs 12.0% in AI arm when tumors have moderate or high levels cyclin D1 expression (p = 0.054).

Conclusion: HR+ breast cancers with co-expression of HER2, cyclin D1, low level HR − less sensitive to neoadjuvant endocrine therapy a, namely, to TAM.

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Feasibility Study of Adjuvant Chemotherapy with S-1 for Advanced Breast Cancer After Primary Systemic Chemotherapy

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Background: Primary systemic chemotherapy (PSC) for advanced breast cancer has been performed preoperatively as standard treatment in late years. Although in cases which were pathological complete response (pCR), they might be better in survival benefit, we often experience non-pCR cases, and they have higher risk to recur postoperatively. Therefore, the new therapeutic strategy that could expect the improvement of treatment effect is mandatory for advanced breast cancer. In this study, we conducted a feasibility study using S-1 as postoperative adjuvant chemotherapy for curatively resected advanced breast cancer patients after PSC.

Material and Methods: Patients with stage II or III breast cancer who underwent anthracycline and/or taxan based PSC followed by surgery were enrolled in this study. Adjuvant chemotherapy consisted of eighteen courses (2-week administration and 1-week withdrawal) of S-1, at 100–120 mg/body per day. From September 2007 to April 2010, forty patients from 2 institutions were enrolled in this pilot study. In cases judged to require postoperative radiotherapy, the concurrent administration was permitted. If they were estrogen and/or progesterone receptor positive, endocrine therapy was permitted concurrently, and if they were human epidermal growth factor receptor 2 positive, trastuzumab was also administered concurrently. The primary end point was successful execution rate of the administration of S-1 for eighteen courses (one year).

Results: Thirty-eight patients were eligible. In 5 patients, S-1 administration was discontinued due to recurrence. Among the 33 patients without recurrence, the planned eighteen courses of S-1 were administered to 21 patients (63.6%). In 7 patients, S-1 administration was discontinued due to subjective symptoms, such as nausea or anorexia. Adverse reactions such as neutropenia, leukopenia, thrombocytopenia, anemia, elevated liver function, anorexia, general fatigue, diarrhea, nausea, and stomatitis were comparatively frequent. Although grade 3 neutropenia (10.0%), leukopenia (7.5%), and diarrhea (5.0%) were observed, no grade 4 adverse effects appeared.

Conclusions: Postoperative administration of S-1 for one year seems feasible as adjuvant chemotherapy for advanced breast cancer after PSC.

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Comparative Study of Breast MRI and Ultrasonography for the Residual Tumor Extent and Response Monitoring in Breast Cancer Patients Undergoing Neoadjuvant Chemotherapy

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Background: To decide the surgical procedure and postoperative treatment clinically, it is necessary to assess the response to cytotoxic drugs acurrately in breast cancer patients undergoing neoadjuvant chemotherapy (NAC).

Materials and Methods: We examined 49 patients undergoing NAC for locally advanced breast cancer between July, 2008 and February, 2011. All underwent MRI and USG prior to NAC and after NAC. We compared residual tumor extent on MRI and USG, with pathological results, to investigate effectiveness of MRI rather than USG. The residual tumor response on MRI and USG was based on RECIST (version 1.1). Analysis was performed using T-test and Spearman's correlation coefficient.

Results: MRI examination of patients completing NAC revealed that 7 patients had complete remission(CR), 25 patients had partial remission(PR), 8 patients had stable disease(SD), and 9 with progressive disease(PD). 4 patients had CR, 32 patients had PR, 8 patients had SD, 5 with PD on USG. Specificity was 90.8%, sensitivity was 81.6%, and accuracy was 86.2% on MRI. Specificity was 72.7%, sensitivity was 86.8%, and accuracy was 79.8% on USG. Spearman's correlation coefficient were 0.731 on MRI, and it was 0.271 on USG. There is no statistical significance in comparison residual tumor extent MRI and USG, compared with pathological results on t-test($p > 0.05$).

Conclusions: Accuracy and Spearman's correlation coefficient on MRI were higher than USG during comparing pathologic results on the residual tumor size after NAC. MRI tends to be more precise for the assessment of residual tumor extent in advanced breast cancer receiving NAC.