form (pCRF) or, more recently, entered manually into an electronical data capture systems (EDC).

Method: In 2005 a collaboration between researchers of the Dept.OBST&GYN TUMunich and Siemens Medical Solutions developed a method of electronically transferring clinical data gathered at the point of care for use in prospective clinical trials. This single-sign-on patient aware electronic platform for clinical trials has been validated in its whole and is prepared to support the regulatory requirements as specified by FDA's 21 CFR part 11 compliance.

Enabling immediate data transfer, the solution is being tested in a pilot study, the HEDON trial (Trastuzumab-Docetaxel-Neoadjuvant), an investigator initiated phase II trial concerning primary systemic therapy of breast cancer and its translational research part (TransHEDON) evaluating therapy response markers as an essential component of this trial. Both started in February 2006 and are ongoing.

To quantify the benefits of our platform, an integrated evaluation project was performed. For a pre-defined time period, data capture and data management processes were performed paper based and electronically. This allows thorough and critical analysis of all involved processes.

Results: The evaluation project proved that the use of such an integrated electronical platform significantly improves efficiency and enables real-time data availability for clinical trial sites.

Conclusion: This innovative solution offers a scalable, automatic transfer of data between a hospital information system (HIS) and an electronic data capture (EDC) system, overcoming interoperability challenges associated with systems that operate on different technical standards and work within distinct business environments.We consider this integrated system to bevery helpful for implementation of clinical trials into a routine hospital setting. This will increase motivation and enhance the quality of studies.

272 Poster

The experience of capecitabine using in neoadjuvant polychemotherapy for breast cancer treatment II–III stages

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Background: Capecitabine is an oral prodrug that is converted to its only active metabolite, FU, by thymidine phosphorylase. It has been successfully proved in treatment of metastatic breast and locally advanced BC. At present the usage of capecitabine in an operable BC treatment has not been investigated enough.

Material and Methods: 78 primarily-revealed patients with II–III stages of BC (T1−3 N0−2M0), aged from 39 to 68, were enrolled. 1 group – 38 patients were treated with scheme CMC: capecitabine (2000 mg/m^2 on days 1−14 per os), cyclophosphan (200 mg/m^2 on days 1−14 i.m.), metotreksat (40 mg/m^2 on days 1 and 8 i.v.), with 14-day interval between cycles. In total the patients received 87 cycles. 2-nd group – 40 patients were treated with scheme CAC: capecitabine (2000 mg/m^2 on days 1−14), cyclophosphan (200 mg/m^2 – day 1−14 i.m.), and adriamicyn (30 mg/m^2 on days 1 and 8 i.v.), with 4-week interval between cycles. In total 110 cycles. All the patients (from two groups) were received to 2−4 cycles of chemotherapy in condition of the dispensaries. The direct efficiency was estimated on scale RESIST, toxicity – on CTC-NCIC.

Results: efficiency on the sum of full and partial regresses was: for group CMC – 68.3%, total regress – 5.3% (2), full morphological regress – 1 case, partial regress – 63.2% (24). Stabilization of process was registered in 28.9% (11) supervision, while progress was noted in 2.6% (1). In group CAC the direct efficiency was: 75%, total regression – 10% (4), full morphological regress in 2 cases, partial regress – 65% (26). The effect received allowed to hold conservative surgery in 50% (CMC) and 47.5% (CAC). The results of treatment were relatively satisfactory. The main difficulties were: a nausea/vomiting (1−2 grade) – 55% (CMC) and 46.4% (CAC); a stomatitis (2 grade) – 17.2% (CMC) and 21.8% (CAC); leukopenia (1−2 grade) – 43.6% (CMC) and 40% (CAC); leukopenia (2 grade) – 2.3% (CMC) and 1.8% (CAC); enteritis (2 grade) 1.1% (CMC); leukopenia (3 grade) – 11.4% (CMC) and 9% (CAC). During treatment the influences of chemotherapy on cardiovascular system was not registered.

Conclusions: The usage of neoadjuvant polychemotherapy under schemes SMH and SAH is satisfactory and effective treatment which enables to increase quantity conservative surgery operations of patients with II−III BC stages.

273 Poster

Antitumor properties of bisphosphonates and possible prevention of bone metastases in breast cancer

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Background: Developing bone metastases (mets) is a devastating event for patients (pts) with breast cancer (BC), placing them at risk for potentially debilitating skeletal-related events (SREs). Bisphosphonates (BPs) have established efficacy for the prevention of SREs in pts with bone mets; preclinical and preliminary clinical data suggest possible antitumor effects of BPs and potential bone mets prevention.

Material and Methods: Data from recent publications and congress presentations were compiled and evaluated, and the status of ongoing clinical trials of BPs for the prevention of bone mets from BC was reviewed.

Results: Initially, antitumor effects of zoledronic acid (ZOL) were identified in preclinical studies. ZOL inhibits tumor cell viability and impedes invasion and adhesion of human BC cell lines to soft tissues and bone. ZOL also acts synergistically with chemotherapy (Cx) agents in animal models. ZOL in combination with doxorubicin increased apoptosis in human BC cell lines in vitro and inhibited tumor growth in a mouse xenograft model of human BC. Recent clinical evidence also suggests that ZOL may have antitumor effects. Low-dose ZOL in cancer pts with bone mets reduced serum levels of VEG-F ($P < 0.04$) suggesting an inhibitory effect on angiogenic signaling. In BC pts without evidence of distant mets (N = 172), ZOL administration for 6 mo appeared to reduce the frequency of isolated tumor cells in bone marrow vs pts who did not receive ZOL (13% vs 27%). Furthermore, results from the large, prospective Z-FAST and ZO-FAST trials of ZOL for the prevention of aromatase-inhibitor associated bone loss indicate a trend toward lower disease recurrence in BC pts receiving upfront ZOL vs the delayed group. Several clinical trials are investigating the efficacy of BPs for the prevention of bone mets in BC pts (NSABP-B-34, AZURE, SUCCESS, S0307). The AZURE study will assess the effect of ZOL in combination with adjuvant Cx and/or endocrine therapy on disease-free and bone-mets-free survival in women with stage II/III BC. Preliminary safety data indicate that ZOL does not compromise delivery or dose intensity of adjuvant Cx nor increase the frequency of adverse events. An interim analysis of AZURE will be performed in 2008.

Conclusions: Preclinical and preliminary clinical studies suggest that BPs could potentially prevent or delay development of bone mets in pts with BC. Several large, randomized trials are ongoing to evaluate BPs in this setting.

274 Poster

Fine-needle aspiration cytology for the evaluation of palpable axillary lymph nodes before sentinel node biopsy in patients with breast cancer

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Background: Sentinel lymph node biopsy (SLNB) has now been accepted as standard for staging breast cancer with clinically negative axillary lymph nodes (ALN). However, with the high incidence of ALNs metastases, patients with palpable ALNs could avoid SLNB if the ALNs metastases were detected before SLNB. The aims of this study were to evaluate the value of preoperative fine-needle aspiration cytology (FNAC) of palpable ALN in patients with breast cancer.

Material and Methods: Between Oct. 2004 and Dec. 2007, preoperative FNAC of palpable ALNs was performed in 143 pts. SLNB was performed in patients with negative ALNs FNAC, and ALND for patients with positive ALNs FNAC. ALNs cytological diagnoses were compared with the final axillary pathological outcomes. The sensitivity, specificity, accuracy, negative predictive value and positive predictive value of palpable ALNs FNAC were analyzed.

Results: Among the 143 pts, 86 (60.1%) were positive for ALNs according to both the FNAC and pathology. In 29 pts (20.3%), both were negative. In 28 pts (19.6%), the FNAC was negative, but metastases were found in the final pathology. Overall, the sensitivity, specificity, accuracy, positive predictive value and negative predictive value of FNA were 75.4%, 100%, 80.4%, 100%, and 50.9%, respectively. ALNs metastases could accurately diagnosed with FNAC in 75.4% pts (86/114), and SLNB could be avoided. Nearly half (28/57, 49.1%) of the patients with clinical palpable axillary nodes and negative FNAC had no metastases in the ALNs, and ALND could be avoided with SLNB. The sensitivity for clinical N1 (n = 118), N2 (n = 23) and N3 (n = 2) were 68.9%, 100% and 100%, respectively. The sensitivity for T1 (n = 7), T2 (n = 122), T3 (n = 4) and T4 (n = 11) were 83.3%, 70.2%, 100% and 100%, respectively. The sensitivity for IIa (n = 5), IIb (n = 110), IIIa (n = 17) and IIIb (n = 11) were 75%, 67.5%, 100% and 100%, respectively.

Conclusions: Preoperative FNAC of palpable ALNs is a simple, minimally invasive, and reliable technique for the initial evaluation of ALNs status in patients with breast cancer. 75% of the patients with ALNs metastases could accurately diagnosed with FNAC, and SLNB could be avoided. Nearly half of the patients with clinical palpable axillary nodes and negative FNAC had no metastases in the ALNs, and ALND could be avoided with SLNB.

275 Poster

Accuracy of MRI in predicting pathologic residual disease after neoadjuvant chemotherapy

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Background: The purpose of this study was to assess the accuracy of magnetic resonance imaging (MRI) in predicting residual disease after neoadjuvant chemotherapy.

Methods: A retroapective review from June 2006 to October 2007 included 44 patients with invasive breast cancer treated with neoadjuvant chemotherapy. In these patients MRI was performed after completing chemotherapy and operated less than four weeks after imaging. MRI results were classified as "no response", "partial response" or "complete response". Pathologic response was classified following the Miller and Payne grading and in order to compare it with MRI, G1 and G2 cases were considered as "no response", G3 and G4 as "partial response" and G5 as "complete pathological response". Results of both, MRI and pathology, were classified as coincident or not coincident. Patients' age, pathologic classification, use of taxanes, Her2Neu status and receptor status were investigated as possible factors influencing coincidence between MRI and pathologic diagnosis. The biggest tumoral diameter on MRI was compared to pathologic size of the reamining tumour, when available. SPSS was used for statistical analysis and Chi2 and Fisher's test applied when appropriate.

Results: MRI results were coincident with pathologic results in 23/44 patients (52.27%). MRI sensibility and specifity for detecting complete pathological response were 57% and 75% respectively. Patients age (<50 or >50), use of taxanes and hormonal receptor status did not influence coincidence significantly. However pathologic type (coincidence in invasive ductal carcinoma 61.7%, in lobular invasive carcinoma 20%, $p = 0.02$) and Her2Neu status (coincidence in Her2Neu positvity 88%, in Her2Neu negativity 42.57%, $p = 0.023$) were factors influencing MRI accuracy. A tumoral diameter was given in 30 patients in both MRI and pathology. The median difference between MRI size and pathologic size was 9.4 mm (sd +31.66), p25 = −2, p50 = 11 and p75 = 25 mm.

Conclusion: MRI is able to predict residual breast disease in 52.27% of patients. The coincidence was significantly higher for invasive ductal carcinoma than invasive lobular carcinoma and for Her2Neu positive tumours than Her2Neu negative tumours. MRI tends to overestimate the size of residual tumours with a wide range of uncertainty.

276 Poster

Role of hypovitaminosis D in bone loss in postmenopausal women receiving adjuvant aromatase inhibitors for EBC: results from a prospective Hospital del Mar Bone Health Breast Cancer Study (HMBHBCS)

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Background: In postmenopausal women, aromatase inhibitors (AI) induce alterations of bone mass density (BMD) and bone turnover markers (BTM). The HMBHBC study is an ongoing phase IV study evaluating the characteristics and the effect of bisphosphonates (BP) on BTM, BMD, bone fractures and quality of life in postmenopausal women receiving AI for EBC with previous tamoxifen (TMX+) or without (TMX−) [upfront AI] treatment (Tt).

Material and Methods: Patients are stratified by lumbar spine, femoral neck and total hip to receive open-label Tt with BP, alendronate or risedronate (if osteoporosis [T-score < −2.5] or osteopenia [T-score < −2.0] and 1 major risk factor) or standard calcium and vitamin D (VitD) supplementation (if normal BMD or T-score > −2.0 and no major risk factor). Levels of 25-OH-VitD, N-telopeptide (NTx), bone alkaline phosphatase (bALP) and osteocalcin (OC) are measured at baseline, 3, 12 and 24 months. BMD and thoracic and lumbar spine X-rays are performed at baseline, 1 and 2 years.

Results: One hundred thirty one women have been included so far. 86.5% had low VitD levels(<30 ng/ml), that are known to induce secondary PTH and hence bone loss. These patients received additional VitD supplements, and 81.7% of them achieved normal values at 3 months, increasing the vitD concentration from 15.5 6.2 to 52.1 3.02 ($p = 0.0001$). Patients TMX+ (n = 98) vs. TMX− (n = 33) had BMD values of osteoporosis in 32.2% vs. 32.3%, osteopenia 52.2% vs. 64.5% and normal 15.6% vs. 3.2% respectively. Patients TMX+ had differences in baseline BTM, with lower values of NTx ($p = 0.0001$) and higher values of OC ($p = 0.003$). BTM at baseline and 3 months are shown in the table.

Patients who received Ca plus VitD experienced an increase in BTM, that reached significance for bALP ($p = 0.026$). Patients who received BP and Ca plus VitD had a significant decrease in NTx and bALP.

Conclusions: This study strongly suggests that VitD status should be routinely assayed before starting AI because hypovitaminosis D is highly prevalent in our series. Importantly, additional supplementation of VitD is needed to reverse hypovitaminosis-induced bone loss. Tt with BP clearly decreases BTM whereas untreated AI shows tendency to increase. BMD and fractures at 1 and 2 years will provide more data to further support the need for BP in patients on AI.

Bone turnover markers	Ca-VitD group (n = 51)	p	BP group (n = 32)	p
NTx basal	41.4±15.1	0.067	53.4±26.1	0.001
NTx 3 months	45.9±19.7		38.9±21.6	
bALP basal	12.3±4.2	0.026	13.4±6.9	0.009
bALP 3 months	13.9±4.9		11±3.8	
OC basal	5.5±4.1	0.25	7.6±6.4	0.6
OC 3 months	6.9±3.7		7.2±6.1	

expressed in mean±SD

Thursday, 17 April 2008 12:30–14:30

POSTER SESSION

Ductal and lobular carcinoma in situ

277 Poster

Detection of disseminated tumor cells in bone marrow in patients with ductal carcinoma in situ

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Background: Haematogenous spread of disseminated tumor cells (DTCs) is considered to be the cause of systemic disease progression and is associated with poor prognosis. It is assumed that only invasive cancers shed isolated tumor cells into the bloodstream. However, latest studies indicate that tumor cell dissemination may occur before stroma invasion, i.e. in ductal carcinoma in situ (DCIS) (Husemann et al., Cancer Cell, 2008). Therefore, the purpose of the present study was to assess tumor cell dissemination in bone marrow in patients with DCIS.

Materials and Methods: 152 bone marrow aspirates from DCIS patients were processed with immunocytochemistry. After Ficoll enrichment of 10 ml bone marrow, cytospins were prepared and stained using the A45-B/B3 primary antibody for pancytokeratin. Cytospins were analyzed by experienced cytologists using the ACIS system (Chromavision) according to the ISHAGE evaluation criteria.

Results: 152 patients could be included into this study. 13% of these patients had detectable tumor cells in bone marrow. The number of detected cells ranged between 1 and 2 cells per 2×10^6 mononuclear cells. There was no correlation found between Van Nuys prognostic index or hormone receptor status and tumor cell dissemination. The bone marrow positivity rates in group with Her-2 positive and Her-2 negative tumors were 14% and 11%, respectively.

Conclusions:

1. Tumor cell dissemination occurs as an early step in the metastatic cascade;
2. Isolated tumor cells may already disseminate from preinvasive mammary lesions;
3. The clinical relevance of these cells has to be further evaluated.