171 days; P=0.015). Among patients with nonlytic lesions, multiple event analysis demonstrated a 12% reduction in the risk of skeletal complications for patients treated with zoledronic acid (n=188) compared with 226 pamidronate-treated patients (HR=0.878; P=0.385). Bone marker data for these patient subsets will be presented. Zoledronic acid was well tolerated with a long-term safety profile similar to that of pamidronate.

Conclusions: These data indicate that zoledronic acid is more effective than pamidronate for reducing the long-term risk of skeletal complications in patients with breast cancer, particularly those with at least 1 osteolytic lesion. Zoledronic acid is the only bisphosphonate to show superiority in a direct comparison with the active agent, pamidronate.

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Pre-operative chemotherapy with Navelbine (N) and Anthracycline in Locally Advanced Breast Cancer (LABC): A multicentric Egyptian Phase II trial

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Navelbine and anthracycline are among the most active agents in the management of advanced breast cancer. Several clinical trials have demonstrated the high efficacy of this combination in advanced breast cancer (Pawlicki, The Oncologist 2002; Vici, JCO 2002). We conducted a multicentric phase II study to evaluate the activity in terms of pathological response rate and downstaging of the combination in locally advanced breast cancer.

Patients and Methods: from June 2002, thirty-four consecutive patients (pts) among the 40 planned have been enrolled in the study. Median age: 46 years (29–63), WHO PS: 0–1, median tumor size: 8 cm, clinical TNM staging was T2: 2 pts (6%), T3: 19 pts (56%), T4: 13 pts (38%), N0: 3 pts (9%), N1: 18 pts (53%), N2: 13 pts (38%), all pts were M0. Histological confirmation was performed by biopsy showing SBR I: 4 pts (12%), SBR II: 20 pts (59%), SBR III: 10 pts (29%). The chemotherapy consisted of 3 cycles of the combination of N: 25 mg/m^2 on day 1 & day 8 plus A: 50 mg/m^2 on day 1 or E: 75 mg/m^2 on day 1 on 3 week schedule. All pts were restaged after 3 cycles; pts showing clinical CR or PR received 3 additional cycles of the combination.

Results: twenty-eight pts were evaluable for clinical response and 34 pts for toxicity; 15 pts achieved a partial response and 8 pts a complete response for an overall response of 82%. The primary chemotherapy has allowed an impressive downstaging in these bulky diseases by reducing to 2 cm the median tumour size. Twenty-one pts went under surgery, 9 pts had a pathological complete response. A total of 169 cycles were administered with a median of 5 cycle/pt. The regimen was well tolerated. WHO neutropenia grade 3/4 was seen in 3 pts, one pt experienced grade 3 mucositis and another one grade 3 phlebitis. Nausea vomiting was moderate and alopecia was universal.

Conclusion: our results confirm that navelbine + anthracycline as pre-operative chemotherapy is a very active and safe regimen in locally advanced breast cancer allowing a high rate of pathological complete response.

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Efficacy and tolerability of combination docetaxel and cisplatin regimen in anthracycline pre-treated patients with advanced breast cancer

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Introduction: The combination of docetaxel (DTX) and cisplatin (DDP) is interesting because both of agents are active in metastatic breast cancer and options of systemic therapy in anthracycline pre-treated patients (pts) are limited. The efficacy and safety of DTX and DDP combinations in anthracycline pre-treated patients with locally advanced or metastatic breast cancer.

Material and Methods: 12 pts with advanced breast cancer were treated with combination of DTX (75 mg/m^2 iv d1q3 weeks) and DDP (75 mg/m^2 iv d1q3 weeks). Median age was 55 (range 34–66). One patient was treated because of locally advanced breast cancer, 11 pts because of metastatic disease with median number of metastatic sites 1.5 (range 1–4). All pts were previous treated with anthracycline: 8 as an neoadjuvant treatment, 4 due to metastatic disease. Median number of previous chemotherapy regimen – 1. All of patients were evaluable for toxicity and tumour response. The response was assessed according to WHO criteria.

Results: A total of 72 cycles were given to 12 patients (median 6, range 3–8). The objective response (OR) was observed in 8 patients (67%): CR in 2 patients, PR in 6 patients, SD in 3 patients (25%) and progression of disease (PD) in 2 patients. In the median follow up 13.7 months, median time to progression (mTTP) was 9.5 months. One patient died because of progression. In our group no severe toxicity was observed. The most common (grade 1 or 2) were: nausea and vomiting, asthenia, arthralgia and myalgia, diarrhea, polineuropathy, oedemas.

Conclusions: Combination of docetaxel and cisplatin is effective and safety regimen in anthracycline pre-treated patients with advanced breast cancer.

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Metastases of adenocarcinoma in axillary lymph nodes of unknown origin

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Background: In patients presenting with metastases of adenocarcinoma in axillary lymph nodes, and no evidence of primary cancer on physical and radiological examination, the most probable source of metastases is undetected microfocus of breast cancer. Therefore in such patients, diagnosis of "occult" breast cancer is made. The incidence of the entity ranges form 0.3% to 1.0% of all breast cancers. However, the diagnosis of occult breast cancer does not necessarily mean that the primary focus must be in the ipsilateral breast. The best method of evaluation of such patients is magnetic resonance imaging of the breast. However the method is not universally available.

Objective: To summarize our experience with occult breast cancer patients in whom magnetic resonance was not performed.

Material and Methods: Study group was composed of twenty two patients with diagnosis of occult breast cancer operated on from January 1982 to December 2002 in our Clinic. The patients files were examined for details of treatment and results of pathological examinations.

Results: In 8 cases (36.4%) mastectomy was performed without the diagnosis of primary focus in the breast. In one case surgical biopsy of upper-outer quadrant of the breast revealed the presence of cancer. It was the only case when mastectomy was performed after the breast cancer diagnosis. Altogether, mastectomy was done in 9 women. In remaining 13 cases, mastectomy was not performed. In 63.5% of women (5/8) who underwent mastectomy despite lack of evidence of breast cancer, pathologic examination did not reveal the presence of cancer. In 53.8% (7/13) of women in whom mastectomy was not performed, primary focus was identified in the breast during follow-up. Altogether, the ipsilateral breast was identified as a source of axillary metastases in 50.0% of women from the studied group. In 45.5% of women the primary focus remained undetected. In one patient (4.5%), the primary focus of cancer was found 9 months after mastectomy in the ipsilateral kidney.

Conclusions: In patients with occult breast cancer efforts should be undertaken to identify the primary focus using modern imaging techniques. As mastectomy seems to be a gross over-treatment, more conservative methods of treatment are advised.

250 POSTER

Modalities in the routine use of trastuzumab (Herceptin®) in advanced breast cancer

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Background: Routine treatment of advanced breast cancer (BC) has been monitored in a postmarketing surveillance study in Germany.

Results: Data from 265 patients (pts) from 80 centers have been collected. About 75% of pts (n=196) received trastuzumab (T) plus concomitant chemotherapy (CT) (mainly paclitaxel, docetaxel, vinorelbine or capecitabine), and 69 pts received T alone. Endocrine therapy was administered for 55% of pts in the T alone group and 37% in the T+CT group. Mean age was 55.5 years (range 28–82). Mean time since initial diagnosis of BC was 4.1 yr in the T alone compared to 2.9 yr in the T+CT group. 84% of pts tested HER2 3+ by IHC, others were confirmed for HER2 positivity by FISH. ER/PR was positive in 59% of pts. Some pts had been pre-treated with cytostatic (53%) or endocrine (37%) treatment for advanced BC and with CT (70%) for early disease. Out of 94% of pts with distant metastasis at onset of T therapy, the liver was the most frequently involved organ in the T+CT group (52%). In contrast, T alone pts predominantly suffered from bone lesions (51%). Performance status at study entry was rather impaired with 53% categorized as ECOG 1 and another 21% as ECOG 2/3. Median duration of documented T treatment

was 44 weeks (range 1–104). Most notably, antibody treatment was continued beyond disease progression in 56 pts. Response rates are summarized in table 1.

Table 1

Objective response	T (n=60)	T+CT (n=179)	Pre-treated* (n=123)	Chemo-naïve* (n=112)
CR+PR	50%	62%	58%	65%
CR	17%	15%	11%	18%
PD	18%	16%	20%	14%

*In the metastatic setting.

Toxicity was a rare event in the T alone group with one case each of grade 3/4 nausea, cardiotoxicity and allergic reaction. In the T+CT group, the antibody effects cannot be separated from those of the cytostatic drugs, with only 3 cases of cardiotoxicity (none of grade 3/4) reported so far.

Conclusions: T proved to be effective and tolerable both as a single drug or part of a chemotherapy combination in the community-based routine treatment of advanced BC. In clinical use the administration of T+/−CT or endocrine treatment is safe and widespread. Notably, although lacking evidence, physicians continue to use T beyond progression of disease in advanced BC.

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Prospective multicenter randomized phase III studies of weekly vs standard docetaxel (D2) plus doxorubicin (D4) for 1st line treatment of metastatic breast cancer (MBC)

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Background: Previous phase II studies indicated a greatly reduced hematotoxicity of taxane based regimens given on weekly schedules. Presently, two trials have been initiated which compare the efficacy and toxicity of weekly applied docetaxel to its standard 3-weekly application. In the D2 trial, elderly and unfit patients are randomized to receive single-agent 1st-line treatment with either weekly or 3-weekly docetaxel, while in the D4 trial younger and fit patients receive either a weekly or 3-weekly regimen of docetaxel in combination with doxorubicin.

Patients and Methods: Patients previously untreated with chemotherapy for metastatic disease can be recruited. Eligible for the D2 study are pts >60 yrs or with a Karnofsky performance status (KPS) of 60–80%. Pts are randomized to receive docetaxel either on a 3-weekly (75 mg/m^2 q3wks, arm A) or on a weekly schedule (30 mg/m^2 d1, 8, 15 q4wks, arm B). Inclusion criteria for the D4 study are age <65 yrs or KPS 70–100%. All pts in the D4 study receive doxorubicin (50 mg/m^2) on the first day of treatment in addition to docetaxel given either at a 3-weekly dose of 75 mg/m^2 q3wks (arm C) or at a weekly dose of 35 mg/m^2 (days 1, 8, 15, q4wks, arm D). Treatment is continued until a maximum of 8 cycles, unacceptable toxicity or disease progression. All pts receive standard corticosteroid prophylaxis.

Results: Presently, 38 pts were recruited for each study (D2 median age 70 yrs, KPS 80%; D4 median age 48 yrs, KPS 90%). In the D2 study, 19 pts are evaluable (A 9, B 10). Grade 3/4 leukopenia was observed in 2/1 pts (A). Grade 3/4 non-hematological toxicity included alopecia (8/0), pulmonary toxicity (2/1) as well as nausea, stomatitis, neurotoxicity and fluid retention (1/0 pt each). In the D4 study, 17 pts are evaluable (C 9, D 8). Severe leukopenia (grade 3/4) was observed in 3/2 pts (C) and 5/2 pts (D). Neutropenia-related complications >grade 2 as infection and/or fever occurred in 2 pts (C) and 1 pt (D). Grade 3/4 non-hematological toxicities included alopecia (6/0), pulmonary toxicity and pain (1/1 each), stomatitis and nausea (2/0 each) as well as neurotoxicity and fluid retention (1/0 each).

Conclusion: Preliminary data support the feasibility of both, the weekly and the 3-weekly regimen of docetaxel application either as a single-agent or in combination with doxorubicin. More complete data will be presented at the meeting.

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Letrozole (LE)–Vinorelbine (VIN) as first-line treatment in advanced breast cancer (ABC) patients: Preliminary results of a multicentre Phase II study

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Therapeutic options for ABC consist of chemotherapy (CHT) and hormonal therapy (HT), but site and number of metastases often limit the use of HT in receptor-positive (RE+) patients (pts). Previous studies investigated the possibility of a synergism between the two options, even if considering old drugs. VIN is a semi-synthetic vinca alcaloid with a well documented activity in ABC pts, as well as LE, a second generation, non steroidal aromatase inhibitor which demonstrated an interesting activity, both as first and second line therapy. Aim of the present study was to evaluate the activity of the LE–VIN combination (objective response, OR) as well as the toxicity. One cycle consisted of VIN 20 mg/mq/week iv for 8 consecutive times, followed by 1 week rest, with the simultaneous administration of LET 2.5 mg/day po, without interruption. In the case of OR or stable disease (SD) 1 or 2 other cycles were planned. Till now, 41 RE+ pts have been enrolled. Median age was 67.5 years (53–96). Twenty pts (48.8%) had received tamoxifen as adjuvant therapy and median DFI was 38 months (0–248). Metastatic sites were viscera (29, 70.7%), bone (34.1%) and soft tissue (20, 48.8%). All pts were PS 0/1 at the start of CHT. A total of 424 administrations were delivered, of which 26 were 1-week delayed mainly due to granulocytopenia. G-CSF were administered in 17 pts. At the end of 1st cycle, 33 pts were evaluable for activity: 1 CR (3%), 4 PR (12.1%) and 19 SD (46.3%) were obtained. 22 pts completed the 2nd cycle: 1 CR (4.5%), 10 PR (45.5%) and 11 SD (50%) were observed. Till now, only 18 pts completed also the 3rd cycle: 2 CR, 12 PR (OR 77.7%) and 4 SD were obtained. LE–VIN combination was well tolerated and few Grade 3–4 toxicities were observed: anemia: G3=1, G4=1; flebitis: G3=1; leucopenia: G4=2; granulocytopenia: G3=1, G4=2. No deterioration in PS was observed. At the present, more than half pts are still taking LE as maintenance therapy.

In conclusion, LE–VIN is a feasible and very well tolerated option for ABC pts. OR are most frequently observed after at least two cycles, probably due to pts hormonal status. Low incidence of adverse events allows its use also in elderly pts with visceral metastatic disease.

253 POSTER

Videothoracoscopic talc pleurodesis for the treatment of malignant pleural effusion in breast cancer

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Background: Malignant pleural effusion secondary to breast cancer is a locoregional disease, caused by lymphatic spread. Talc pleurodesis is an effective technique for the management of symptomatic malignant pleural effusion. The aim of this report is to evaluate the results and follow-up in patients undergone videothoracoscopic talc pleurodesis for malignant pleural effusion secondary to breast cancer.

Methods: Forty-four patients underwent videothoracoscopy for malignant pleural effusion secondary to breast cancer. Either cytology on pleural fluid or histology on pleural biopsy obviated final diagnosis of malignancy in all patients. All of these patients were treated with talc pleurodesis performed under general anaesthesia, once the possibility of a complete re-expansion of the lung on the treated side had been ascertained. Five grams of sterile asbestos-free purified talc were insufflated in the pleural space under direct vision at time of the procedure. One chest tube was left in place until the fluid drainage was less than 100 mL per postoperative day. Quality of life was assessed before surgery and at 1 month after procedure by short form health survey (SF-36) and Nottingham Health Profile questionnaires.

Results: No perioperative mortality was observed. Videothoracoscopic talc pleurodesis was effective in controlling recurrence in all patients at 1 month. Two episodes of respiratory distress syndrome were observed. Overall survival at 6, 12 and 24 months was 91%, 73% and 41% respectively. Moreover quality of life was significantly improved in all patients.

Conclusions: Videothoracoscopic talc pleurodesis represents the procedure of choice for treatment of malignant pleural effusion secondary to breast cancer.