95%CI: 3.2–29.1%); nine (29%) pts had stable disease and 17 (54.9%) pts progressive disease. The median TTP was 4.6 months (range, 0.8–43.8) and the median OS 14.4 (range, 21–44.8) months.
Conclusions: The GEM/LOHP is a well tolerated and relatively active regimen for patients with heavily pretreated ABC, achieving a tumor growth control in 44% of the patients.

464 PUBLICATION

A pharmaco-epidemiological study of Trastuzumab therapy in metastatic breast cancer

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Introduction: A large pharmaco-epidemiological Brazilian study was conducted to investigate the efficacy, the treatment duration and the mostly prescribed treatments to patients with HER2 positive metastatic breast cancer (MBC).
Methods: Retrospective data was collected in 3 centers and statistical analysis was performed with a two-sided significant level of 5%. Treatment duration and disease-free survival were analyzed using the Kaplan-Meier method and were compared using a log-rank test.
Results: A total of 121 women range from 26 to 88 years (median = 53yo) with proven cancer breast were enrolled between may/2000 and november/2004. The HER-2 status (N = 110) was IHC 3+ = 93, IHC 2+ = 15, IHC 0–1+ = 2. Hormone receptor status (N = 121) was ER+ 47 and PR+ 36. The median time from diagnosis of primary disease to metastasic diagnosis was 2.2 years, range [0–7.8]. The median time from MBC diagnosis and the first prescription of trastuzumab was 159 days [0.0–2978]. 67% of patients used trastuzumab in first line, 21% in second line and 12% in third or others lines. The mostly used strategy therapy in the first-line was trastuzumab associated with vinorelbine (25.2%) and in the second-line were trastuzumab and paclitaxel (21.4%). In the whole population, the median DFS (defined as the time from initiation of trastuzumb to progression or death related to the disease) was 13.5 months, range 7 days to 4 years. CR was observed in 24.5%. No statistical difference on the treatment duration was found comparing patients who received his first course of trastuzumab on first or second-line ($p > 0.05$). The treatment duration in patients who received the first course of trastuzumab on first-line was much higher than among patients who received just on third-line and beyond ($p = 0.01$). The disease free survival for patients who received trastuzumab treatment in first-line was significant higher than patients who received his first course of trastuzumab on second-line ($p = 0.025$) IC: 94% and much higher than the group who received firstly on third and other lines (de $p < 0.0001$). No death was related to trastuzumab events.
Conclusion: We can conclude in this real-life model of analysis that trastuzumab shows greater benefits when used firstly in first-line, as we see in published randomized clinical trials results.

465 PUBLICATION

Male breast cancer: our experience from 1990 to 2004

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Male breast cancer (MBC) is a rare disease which accounts for less than 1% of all breast cancer cases. Approximately 400 new cases of MBC are diagnosed in Italy each year. We performed a retrospective analysis of 48 cases of MBC diagnosed since 1990, in order to analyse the pathological characteristics of the disease. The average age of these patients was 60 years (range 37–84). Forty-two patients had a diagnosis of ductal carcinoma; the others were: papillary 2, intraductal 2, lobular 2. High grade (G2-G3) tumors were present in 27 patients. Three patients were stage IV; 12 patients were stage III and 15 and 13 were stage II and I respectively; 36/48 (75%) patients were oestrogen or progesterone receptor positive, 4/48 (8%) patients were hormone receptor negative; in 8 patients oestrogen and progesterone receptors were not known. Thirty-one of the patients (65%) were treated with chemotherapy and anti-oestrogen therapy; 8 patients (17%) with anti-oestrogen therapy alone. Conservative surgery was performed in one patient only, while all the others underwent mastectomy (97%). Twenty (42%) had recurrences after treatment. Sites of relapse were: 8 visceral (17%), 5 bone (10%), 10 soft tissues (21%); local recurrence occurrence in 2 patients (4%).
BRCA1/2 mutational analysis was performed in 11 patients and two of them from high risk families, were identified as carriers of a BRCA2 mutation.
Conclusion: Thus, in our series, men with breast cancer are slightly younger, more likely to have hormone receptor positive disease, nodal metastases, and advanced stage disease than women with breast cancer. MBC patients should be offered genetic counselling and BRCA genetic testing when members of a high risk family.

466 PUBLICATION

A Phase II trial of gemcitabine (G) and doxorubicin (D) combination as first line treatment of metastatic breast cancer: preliminary results

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Methods: Previously untreated female patients (pts) with visceral metastatic breast cancer and ECOG PS $\leqslant 2$ were included. Pts received D 25 mg/m^2 and G 1250 mg/m^2 on days 1 and 8 for both drugs, every 21 days until progression or severe toxicity.
Results: 32 pts with a median age of 44.1 years (range: 29–67) were enrolled. All pts had stage IV disease. Metastatic sites are detailed in the table below. 31 patients were evaluable for toxicity and 26 patients for response. One patient has voluntary interrupted treatment after one cycle. After 178 cycles, grade 3 and 4 toxicity (WHO) were: neutropenia (4%), febrile neutropenia (0.5%), anemia (1.5%), nausea and vomiting (16%), diarrhea (2%), mucositis (11), reversible alopecia (56%). Among the 26 evaluable patients, response rates were: complete response 27% (7 pts), partial response 23% (6 pts), stable disease 8% (2 pts) and progression 42% (11 pts).

Metastatic sites

Metastatic sites	Number of pts	%
Liver	20	62.5
Lung	13	40.6
Bone	14	43.7
Lymph node	3	9.3
skin	1	3.1
*3 organs involved	2	6.25

Conclusions: The combination of GD in untreated metastatic breast cancer appears to be an active regimen with a safety toxicity profile. Further follow-up is necessary to assess the efficacy of this regimen.

467 PUBLICATION

Pegylated liposomal doxorubicin (PLD) plus cyclophosphamide as 1st-line therapy for metastatic breast cancer in patients previously treated with anthracyclines

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Background: Anthracyclines are among the most active drugs used for the treatment of breast cancer. Utilization in advanced disease however, is limited by their intrinsic dose limiting cardio-toxicity and extensive exposure in the adjuvant setting. Pegylated Liposomal Doxorubicin (Caelyx/Doxil) has been shown to possess similar activity to conventional doxorubicin, with a more favorable toxicity profile and significantly less cardiotoxicity. Cyclophosphamide is commonly used in combination with anthracyclines, thus represents an interesting drug to use with PLD.
Methods: We undertook a multi-center single arm Phase II trial to assess the safety and efficacy of PLD 35 mg/m^2 in combination with cyclophosphamide 600 mg/m^2 every 3 weeks. Eligibility criteria included: Measurable disease, prior anthracyclines exposure > 12 months prior to study entry, adequate organ and bone marrow function.
Results: Fifty-one patients have been enrolled, median age 53 years old (38–77). All patients had previously receive anthracyclines either doxorubicin (64%) or epirubicin (36%) at a median dose of 240 mg/m^2 or 600 mg/m^2, respectively. Some patients also received cyclophosphamide (83%), 5-Fu (30%) and taxanes (20%) as part of their adjuvant therapy. A median of 6 cycles (2–10) of chemotherapy were delivered and no major toxicity has been reported after the first 40 patients. Four patients experience asymptomatic >10% declines in LVEF that was reversible upon discontinuation of PLD. The incidence of hand foot syndrome (HFS) was relatively low (13%); only one patient stopped therapy due to grade 3 HFS. Other toxicities were uncommon and usually did not lead to discontinuation

of therapy. The efficacy analysis revealed a 36% objective response rate with another 28% of patients having disease stabilization.
Conclusion: The combination of PLD with Cyclophosphamide given every 3 weeks is a safe and active combination in advanced breast cancer patients who relapse more then one year after completion of adjuvant therapy with anthracyclines.

468 PUBLICATION

Safety and efficacy of first-line docetaxel (DXL) – gemcitabine (GMZ) in metastatic breast cancer (MBC)

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Purpose: New combinations and strategies have been developed over the past 10 years including new drugs such as taxanes and gemcitabine and this design demonstrates the feasibility of the most effective drugs, while minimizing toxicity. DXL–GMZ has shown significant activity against mbc in a lot of studies.
Methods: from November 1998 to January 2000, 42 patients have been enrolled in the study and all patients had previously received adjuvant therapy.
Treatment: Patients received DXL: 75 mg/m^2 day 1+GMZ: 1250 mg/m^2 day 1 and day 8, every 3 weeks without growth factor support. median age was 57.5 years (range 27–74).
Results: Complete response was observed in 22.5% (9 patients) and partial response in 57.5% (24 patients) with an overall response rate of 80%. The probability of one-year survival was 83.5%. Main grade * toxicities were Neutropenia in 12.5% (5 patients) and Anaemia in 7.5% (3 patients). Nausea and vomiting grade 2–3 were in 19.2%.
Conclusion: DXL + GMZ is an active regimen in mbc. This scheme is of an easy administration, very well tolerated and effective in patients with MBC relapsing after an anthracycline based adjuvant treatment.

469 PUBLICATION

Allogeneic hematopoietic cell transplantation for metastatic breast cancer

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To describe the efficacy of allogeneic hematopoietic cell transplantation for metastatic breast cancer, we reviewed registry data from 16 centers participating in the Center for International Blood and Marrow Transplant Research and the European Group for Blood and Marrow Transplantation between 1992 and 2000. Probabilities of transplant-related mortality (TRM), graft-vs-host disease (GVHD), disease relapse or progression, progression-free survival, and overall survival were determined. Seventy-five patients were identified from the registries; median age at transplant was 41 years (range, 25–60) and the median follow-up time for survivors was 25 months (range, 3–64). Thirty-nine patients (52%) received myeloablative conditioning regimens and 36 (48%) were given reduced-intensity conditioning (RIC) regimens. Patient characteristics were similar between the two groups except that more patients in the RIC group (72%) had low performance status than did those in the myeloablative group (26%). More patients in the myeloablative group had acute GVHD (46% vs 33% in the RIC group) at 100 days, chronic GVHD at 1 year (39% vs 8% in the RIC group), and 100-day TRM (26% vs 7% in the RIC group). Overall response rates (complete or partial response) were 31% for the myeloablative group and 29% for the RIC group. Nine of 38 patients (24%) who underwent immune manipulation after transplant showed disease control, providing direct evidence of a graft-vs-tumor effect. Further, multivariate analysis showed that the presence of acute GVHD after an RIC regimen reduced the risk of disease relapse or progression but did not affect progression-free survival.
The presence of disease control in association with acute GVHD suggests the existence of a graft-vs-tumor effect in heavily pretreated metastatic breast cancer patients.

470 PUBLICATION

Interim analysis of a Phase II study of biochemotherapy in metastatic breast cancer (MBC)

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Background: Breast cancer is moving on from being lethal, towards chronic, owing to the availability of targeted therapy.
Objective: To determine the response rate, time to disease progression and overall survival.
Methods: Women were eligible if they were; histological confirmed invasive infiltrating carcinoma, HER-2/neu FISH positive MBC. PS 0–2 with adequate renal, liver and hematological functions. Trastuzumab was given 4 mg/kg loading dose then 2 mg/kg and vinorelbine 25 mg/m^2 weekly. The regimen was continued until progression of disease or undue toxicity experienced or patient herself withdraws consent.
Results: We have thus accrued 25 patients, mean age of 53 yrs. The first line in 08%, second line in 32%, third line in 48% and fourth line 12% of the cases. Over half of patients had bony metastases; single visceral metastatics were present in 24%, multiple visceral metastatics were present in 48%. The overall response was 72% and stable disease was observed in 12%, progressive disease in 16% of the cases. Time to disease progression and survival data will be mentioned in the final analysis. Five grade-3 toxicities, including two cardiomyopathies were noted.
Conclusion: Bio-chemotherapy with weekly Trastuzumab in combination with Vinorelbine yields an impressively high response rates, with acceptable toxicity profile in this ongoing Phase II study in metastatic breast cancer in Pakistani Women. We caution that this is an interim analysis, and final data will be available in about two years.

471 PUBLICATION

Letrozol in the treatment of metastatic breast cancer

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Background: The aim of the stady is to establish the treatment power of Letrozole in women with metastatic breast cancer.
Patients and methods: Forty four postmenopausal women mean age 59 years were included in the stady. Distribution of the patients by stages is: 20.4% operated in stage I, 45.5% – in stage II, 22.7% – in stage III, and 11.4% have been diagnosed in stage IV. The last group of patients had cyological confirmation of the disease only. Histologicaly there were 30 invasive ductal, and 9 invasive lobular cancers. All of the patients had positive hormonal receptors, except of the 5 nonoperated patients (unknown receptors). Adjuvant therapy included anthracycline containing chemotherapy FEC (Farmorubicin, Cyclophosphamide, 5-FU) in standard doses in 31.8% of the patients, CMF (Cyclophosphamide, Methotrexate, 5-FU) – 31.8%, CNF (Cyclophosphamide, Novantrone, 5-FU) – 6.8%. Most of the patients received Tamoxifen (79.5%). Twenty nine patients (65.9%) had metastatic disease in one organ or system, and 15 (34.1%) – in two or more organs or systems. Twenty five patients (56.8%) had bone metastases, 16 (36.4%) – soft tissue metastases, 9 patients (20.5%) – lung metastases, and 9 patients (20.5%) had liver metastases. Twenty patients (45.4%) received Letrozole as a first line therapy for metastatic disease, 54.6% – as a second line after chemotherapy. The mean treatment duration was 12.63 months (5–13 m.) in dose 2.5 mg/d.
Results: Letrozole was very well tolerated. ORR was 63.6% including 2 CR (soft tissue metastases), 4 PR (1 patient with soft tissue metastases, 1 with lung metastases, 2 patients with liver metastases), and 34 SD with improvement of Karnofsky PS. Four patients (9.1%) with more than one metastatic site had progressive disease. Survival data are expected.
Conclusion: Letrozole is a high power aromatase inhibitor for the treatment of patients with metastatic breast cancer, including those with asymptomatic visceral metastases.

472 PUBLICATION

Preoperative chemoradiotherapy of locally advanced breast cancer

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Purpose: To assess the efficacy of neoadjuvant chemotherapy and accelerated radiotherapy in breast cancer patients by evaluation of postoperative morphological changes.
Methods and materials: Between March 2001 and March 2005 31 patients with stage IIB-III breast cancer were treated. For majority, the induction chemotherapy consisted of two-four courses (doxorubicin or epirubicin, cyclophosphamide and 5-fluorouracil, on the first day of a 21-days cycle – 21 patients). 10 pts were treated by two drugs: paclitaxel