bocytopenia; non-hematological toxicity consisted of mild fluid retention in one patient and a G3 skin reaction in another one. Partial responses were found in 7 pts, stable disease in 3 and progressions in 4.

Conclusion: our experience confirms that docetaxel is an active drug (50% response rate), well tolerated in paclitaxel-pretreated advanced breast cancer patients.

1312 PUBLICATION

Tolerance and efficacy of high dose doxorubicin in a sequential neoadjuvant regimen for locally advanced breast carcinoma (LABC): Preliminary results of a phase II trial

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Background: Treatment of LABC requires more efficient systemic treatments for better disease control. Sequential dose intense regimens are new strategies developed trying to improve current response rates and survival.

Purpose: To evaluate the efficacy and tolerance of High Dose Doxorubicin followed by a combination of Cyclophosphamide and 5-Fluoruracil in a sequential intense neoadjuvant regimen in a prospective phase II trial. We presented an interim analysis of toxicity and efficacy data for the first 44 pts. who received the intensified Doxorubicin treatment.

Methods: Treatment plan consisted of 3 to 4 courses of Doxorubicin 90 mg/sqm divided in 3 days (iv push) every 3 weeks followed by 3 or 4 courses of Cyclophosphamide 1 gr/sqm on day 1 iv push and 5 Fluoruracil 1 gr/sqm daily for 3 consecutive days as 2 hours iv infusion. No hematopoyetic growth factors or cardioprotector agents were allowed. After primary treatment, responsive patients underwent surgery or locoregional radiotherapy.

Results: From June 1996 to June 1997, 44/48 pts. are evaluable. Median age was 47.2 years (32–69), with 61.3% of premenopausal; 42 pts. completed 3 courses of therapy and 12 pts underwent a 4th course. Objective response after Doxorubicin treatment was 79% (IC 95% 68.3–91.4%) with complete response in 23.2% and partial in 55.8%. The relative dose intensity was 0.87 (26.2 mg/sqm/week). Grade 3–4 hematological toxicity occurs in 19 pts. (47.5%) but only 5 cases of febrile neutropenia. One pt. was off study due to severe toxicity but no treatment related deaths or significant cardiotoxicity was observed.

Conclusion: Our data shows that High dose Doxorubicin is a safe and well tolerated regimen with moderate hematologic toxicity and no cardiac toxicity in spite of the dose intensity of the treatment with also impressive high antitumor activity. Further evaluation of the full regimen will clarify the impact of this sequential dose intense strategy in LABC.

1313 PUBLICATION

Post-irradiation sarcoma (PIS) in patients treated for breast cancer: A retrospective study of the BCNIRTOG-Italy

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Purpose: There are several reports in the literature on the development of sarcomas after irradiation for breast cancer (BC). Moreover, an increase of the risk of developing a soft tissue sarcoma in BC patients is reported. The aim of this retrospective study is to quantify the risk of developing a PIS in a population of patients treated in the Centers collaborating at the Breast Cancer North Italy Radiation Therapy Oncology Group (BCNIRTOG).

Methods: All the PIS registered in the 23 Radiation Oncology Depts. collaborating at the BCNIRTOG, annually treating about 3000 patients with BC, were collected.

Results: 17 cases were observed, 12 arising after breast conservation and 5 in the chest wall for an incidence of less than 0.1%. The histology was: angiosarcoma, 10; fibrosarcoma 2; malignant histiocytofibrosarcoma, 2; sarcoma nos, 2; condrosarcoma, 1. Age at diagnosis ranged between 25 and 76 years (median 48 years). The PIS developed 18–324 (median 120) months after irradiation (range 25–60.25 Gy, median 54 Gy). All the patients treated conservatively for the first tumor had a mastectomy: 11 are alive without disease, one developed a local recurrence and lung metastases and is dead. The 5 mastectomized patients had a local complete excision of the second tumor, one had a local recurrence (lost at follow-up) and one distant metastases.

Conclusion: In our experience the development of a PIS are BC is an extremely rare occurrence. In this series the poor prognosis of PIS is not confirmed. Surgery played an important role m the outcome of these patients.

1314 PUBLICATION

Cytokines in anticancer therapy in advanced and metastatic breast cancer

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Purpose: It is known, advanced and metastatic breast cancer is treated without significant positive results. Therefore we tried to use cytokine TNF-α and IFN reducer ds-RNA in breast cancer therapy.

Methods: TNF-α was used in complex therapy in 9 pts with advanced and metastatic breast cancer. All pts had metastases in bones, 4 pts (44.4%) had also metastases in lung, skin, lymph nodes and opposite mammary gland. TNF-α was used i.v. in dose n + 0.5 $\times$ 10^6 IU/daily (n = 10^6IU). The daily dose was escalated till 3 $\times$ 10^6IU. The total course dose of TNF-α was 3-x10^6IU. IFN inducer ds-RNA ("Ridostin") was used in dose 8 mg i.m. every other day (the total course dose was 48 mg). There were from 3 to 6 courses.

Results: Pr- 3 pts (33.3%); SD-6 (66.7%). Morphological examination of minor tissue from mamma gland and regional lymph nodes has shown extensive multiple necrosis in cancer tissue. Sorrounded tissue was infitrated with lymphocytes and neutrophils. In peripheral blood we have observed positive changes.

Conclusion: We conclude that using of cytokines in breast cancer therapy is effective. We can recommend to use TNF-α and interferon inducer in advanced and metastatic breast cancer treatment.

1315 PUBLICATION

Weekly combination of taxol, 5-fluorouracil and leucovorin (TFL) in advanced pretreated breast cancer patients

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The activity of TFL combination every 3 weeks has been demonstrated in an our previous study with a response rate of 47.5% (Nisticò, 9th International Congress on Anticancer Treatment '99) as well as the feasibility and safety of weekly 1-hour infusion of Taxol (Seidman, Seminars Oncology '97). With the frequent administration of shorter infusions there may be cytokinetic advantages to the dose-dense scheduling by reducing the interval between cycles. Since May 1998 24 advanced pretreated breast cancer patients were treated with taxol 80 mg/sqm/wk as 1-hour infusion, 5-fluorouracil 300 mg/sqm/wk plus 1-folinic acid 10 mg/sqm/wk for 24 consecutive weeks in the absence of progression. G-CSF was included in treatment schedule on days 2 and 4 to allow the full delivery of a dose-dense weekly schedule. Patient data: median age 54 years (range 39–70; PS 0–1/2–3: 21/3 pts; pre/postmenopausal status 1/23 pts; ER+/– 16/6 pts, 2 unknown. Metastatic site: bone 7 pts, soft tissue 8, viscera 9. All patients had received previous anthracyclines. TFL was delivered as first line metastatic treatment in 6 patients, as second line in 12 and as third line in 6 patients.

Results: toxicity (WHO) was evaluated in 257 courses (c): anemia G2 12 c (3 pts); no other hematological toxicity was observed; vomiting (G3) 1 c, stomatitis (G2) 1 c, severe asthenia 6 c (2 pts). No patient experienced peripheral neuropathy, diarrhea or cardiac toxicity; one patient had an hypersensitivity reaction. Seventeen pts are evaluable for response to now. A complete response was observed in 1/17 (6%), partial responses in 10/17 (59%), stable disease in 2/17 (11.5%) and progression in 4/17 (23.5%) for an objective response rate of 65%.

Conclusion: the excellent toxicity profile and the good activity in this group of unfavourable prognosis patients warrant further extension of this weekly experience.