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CLINICAL RESPONSE IS NOT A GOOD PREDICTOR OF HISTOLOGICAL RESPONSE IN BREAST CANCER NEOADJUVANT CHEMOTHERAPY

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Efficacity of neoadjuvant chemotherapy (NAC) in breast cancer is often judged on the clinical response. Between 1988 and 1992, 71 patientes with advanced cancer were treated by NAC: stades IIA (2 ptes), IIB (9), IIIA (16), IIIB (39), and stade IV (5). Histological grades : I (3), II (19), III (28), unknown (22). Estrogens receptors were: ER+ (29), ER- (19), unknown (22). Median tumor size was 6,7 cm. Several schedules were used, all with an anthracycline: FAC(21cases),FEC(29),FNC (19), FTC (2). The clinical response was evaluated by physical examination. All patients were surgically evaluated by modified mastectomy (52 cases) or tumorectomy (19), always with an axillary lymph node dissection after four or six cycles.

RESULTS: Clinical responses were: Complete (CCR): 25 (35%), Partial (PCR > 50%): 24 (34%), and Stable disease: 22 (31%). Histological responses were: HCR: 9 (13%), HPR: 24 (34%), and HSD: 38 (53%). Lymph node involvement: N-: 21 (29%), N<75%: 28 (38%), and N>75%: 22 (30%). HCR were always N-. For CCR , HCR was found only in 4 cases (16%), and HSD in 13 cases (52%). N- was found in 8/25 CCR, and N>75% in 7/25 CCR. Although a short follow up for many patients we observed 15 metastatic evolutions: only one in a HRC, but 14 in HPR, HSD, or N+(p<0,05).

CONCLUSIONS: clinical response is not predictive of the histological response. Lymph nodes involvements after neoadjuvant chemotherapy have a predictive value for evolution.

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MITOXANTRONE AND METHOTREXATE (MM) IN ELDERLY PATIENTS WITH METASTATIC BREAST CANCER

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Twenty-three patients over 70 years with advanced or metastatic breast cancer who had not received prior chemotherapy, were treated with mitoxantrone 12 mg/m^2 and methotrexate 40 mg/m^2 on day 1 every 3 weeks.
Till now 19 pts were evaluable for response. We observed (according WHO/UICC) 8 PR (42%), 5 NC (26%) and 6 PD (32%).
Median duration of response was 6.5 months.
All 23 pts were evaluable for toxicity. Maximal toxicity (WHO-criteria): leucopenia GI-II 8 pts, GIII-IV 7 pts; thrombocytopenia GI 2 pts, GIII 2 pts; alopecia GI 8 pts, GII 4 pts, GIII 5 pts; mucositis GI 4 pts, GII 1 pt.
In 14 pts nausea/vomiting without use of antiemetic therapy was recorded: G0 6 pts, GI 4 pts, GII-III 4 pts.
MM appears to be an effective and well tolerated chemotherapy in elderly patients with metastatic breast cancer.

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MEGESTROL ACETATE (MGA) PLUS ALPHA 2A INTERFERON (IFN) AS SECOND LINE THERAPY IN PATIENTS (pts) WITH ADVANCED BREAST CANCER (a.b.c.): PRELIMINARY RESULTS OF A MULTICENTRIC PHASE II TRIAL

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MGA, has been assessed usually after tamoxifen (tmx) treatment, showing an overall response rate (RR) ranging from 20 to 30%. An improvement of activity could derive from IFNs, that are known to both up-regulate ER and PgR levels in breast cancer cell lines and to synergize with antiestrogens and progestins in inhibiting cell growth. A multicentric phase II trial was started. Up to now 28 evaluable postmenopausal pts with a.b.c., initially responsive to tmx treatment either as adjuvant or palliative treatment were treated with MGA (160 mg/day p.o.) and Alpha 2a IFN (3 x 10^6 U.i. 3 times weekly i.m.). Characteristics of pts were: median age 64 years (range 40–76); dominant site of metastasis: soft tissue in 6 pts (21.5%), bone in 15 pts (53.5%) and viscera in 7pts (25%); ER status was positive (> 10 fmol/mg) in 12 pts (43%) and unknown in 16 pts (57%). 20 pts have been given tamoxifen as adjuvant treatment, while 8 have received no adjuvant therapy; tmx (± ct) for metastatic disease was administered to 20 pts. Objective responses were observed in 5 pts (18.5%, 95% CI=3.5%–33.5%): 1 pts showed a CR of bone metastasis, and 4 pts a PR of bone (1 pt) and of soft tissue lesions (3 pts). SD was observed in 14 pts (52%), and PD in 8 pts (29.5%). Major toxicities included flu like syndrome (with fever grade 1–2 in 13 pts, chills and astenia) in 26 pts (92.8%), nausea (grade 1) in 5 pts (17.8%), vomiting (grade 2) in 2 pts (7.2%), anorexia and weight loss in 4 pts (14.2%, with a median weight loss of 3 kg, range 2–3), alopecia in 1 pt (3.6%), leukopenia (grade 2) in 2 pts (7.2%); weight gain occurred in 5 pts (17.8%, with a median gain of 4 kg, range 2–8). The response rate obtained by the combined treatment is superimposable to that usually achieved with MGA alone, while an increased toxicity was observed. In conclusion, the role of IFN in the treatment of breast cancer remains to be further defined.

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COMPARISON OF SALVAGE CHEMOTHERAPY PROTOCOLS IFOSFAMIDE+MESNA+ETOPOSIDE VERSUS IFOSFAMIDE+MESNA+EPIRUBICIN IN CASES WITH STAGE IV BREAST CARCINOMA.

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We have administered Ifosfamide+Mesna+Etoposide (Group I) and Ifosfamide +Mesna+Epirubicin (Group II) as salvage chemotherapy to 38 patients with STAGE IV BREAST CARCINOMA. Group I consisted of 25 female patients and Group II consisted of 13 female patients. In group I,we observed observed complete response in 8% and partial response in 52% and progressive disease in 36 % of the patients.In group II,partial response was 69% and progressive disease was 31%.The mean remission period was 12 months and 9 months,respectively.The difference between the remission periods, was not significant.There was no significant difference between the effect on neither overall survival nor disease free survival.When the two groups were comparied according to the dominant metastasis region,no significant difference was found.However in patients of second group with visseral and bone metastasis, we have observed that the response to the therapy was better. In both groups the complications of the therapy were alopecia,nausea, vomitting, neutropenia and thrombocytopenia. Serious complications such as renal and hepatic dysfunction and cardiac toxicity, which requires discontinuation of the chemotherapy were not seen. As a result,these chemotherapy protocols can be used in patients with stage IV breast carcinoma.

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NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CARCINOMA

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Forty patients with locally advanced breast carcinoma were treated with neoadjuvant chemotherapy (NCT).
17 pts. (1987-89) recieved CNF (CTX 600mg/m2, MT 12 mg/m2 and 5FU 600mg/m2) and 23 pts. (1989-92) had CAF regimen (CTX 500 mg/m2, ADM 50mg/m2 and 5FU 500 mg/m2). In 20/40 pts. (50%) total mastectomy and axillary sampling was performed after chemotherapy. Radiotherapy was administred to 12 pts. as definitive treatment after chemotherapy and to 17 pts. after radical operation. The two treatment regimens were compared:

	CNF Group	CAF Group
Overall response to NCT	11 pts. (53%)	9 pts. (39%)
Clinical CR after NCT	2 pts. (12%)	2 pts. (8%)
Radical operation	7 pts. (41%)	13 pts. (56%)
Pathologic CR	0 pts. (0%)	1 pt. (4%)
Progression during NCT	2 pts. (12%)	6 pts. (26%)
Local relapse rate	4 pts. (23%)	2 pts. (9%)
Distant relapse rate	5 pts. (29%)	7 pts. (30%)
2 year actuarial survival	80 %	74%

We conclude that CNF and CAF regimens seem to be equally effective in locally advanced breast carcinoma.

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ACTIVITY OF TAXOL (T) BY 3 H INFUSION IN BREAST CANCER PATIENTS (PTS) WITH CLINICAL RESISTANCE TO ANTHRACYCLINES (A).

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From May to December 1992, we treated with T 15 pts with breast cancer who relapsed within 12 months after adjuvant therapy containing A (n=8), or progressed on A-therapy for metastatic breast cancer (7). T (52 cycles) was given IV in 3 h at 175 mg/m^2 q 3 wks after anti-allergic pre-medication. From the 2nd cycle, the dose was increased (200 mg/m^2) or decreased (150 mg/m^2) according to individual tolerance. Median age was 42 yrs (31-55) and ECOG PS was 0 (0-2). All pts had measurable disease involving breast (5), lymph nodes (12), skin (5), liver (5), lung (5), and bone (2). Hematologic toxicity consisted of Gr 3 (26% cycles, 6 pts) and Gr 4 neutropenia (4% cycles, 1 pt). Other toxicities were hair loss (Gr 3, 15 pts) paresthesias (Gr 1, 14 pts), arthralgias (Gr 1 in 8, and Gr 2 in 2), nausea and vomiting (2 pts). Hypersensitivity to T or cardiotoxicity were absent. Overall, we observed 1 CR and 6 PR (46% RR; 95% C.I. 21-73%), 3 SD (13%) and 5 progressions (33%). The trend for response was similar for patients failing adjuvant A (37% RR) or A therapy for metastatic disease (57% RR). At the selected dose and schedule, T is very well tolerated and active in pts with breast cancer and clinical resistance to A. Since limiting toxicities were not observed, the trial is ongoing at an escalated entry-dose of 225 mg/m^2.