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Ifosfamide,Vincristine, Epirubicin (IVE) as third - line salvage chemotherapy for recurrent anthracycline-naive postmenopausal metastatic breast cancer.

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Patients (pts.) with metastatic breast cancer (MBC) who fail to adjuvant first and subsequently to second-line systemic therapy are difficult to manage and usually candidates to investigational treatments. In a phase II trial we combined Ifosfamide - mesna :2.2 g /m^2(days 1 to 5) iv. , Vincristine : 1.0 mg/m^2 (day 1) iv.,Epirubicin: 35 mg/m^2(day 2) iv. IVE regimen was administered every 4 weeks , until progression , severe toxicity or patient's refusal. From Jan. to Dec.,1992 , 38 postmenopausal pts. with hystologically proven , progressive metastatic breast cancer , not previously treated with anthracycline - containing regimens , median age 56 yrs. (49-68) , median PS 1 (0-2) , with progressive disease in bone (10 pts.), skin (14 pts.)and viscera (16 pts.) received IVE chemotherapy. Previous treatments were as follows : CMF (adjuvant) -----> 5-FU + FA +/- MMC (second line) = 18 pts. and TAM (adjuvant) ------> HD-MPA or AG (second line) = 20 pts. A total of two hundred and twenty seven courses were administered with a median number of 6 courses (range 3 - 9). In 36 currently evaluable pts. , 6 CR and 10 PR were observed , for an overall response rate of 44% (95% C.I.= 33-55%). No significant difference in response rate was observed in relation to previous treatment : previous chemotherapy : 7/16 (44% - 95% C.I.= 32-55%) versus previous hormonetherapy : 9/20 (45% - 95% C.I.= 34-56 %) . Median duration of response was 5.5 months (range 3-9) .Toxicity , assessed on day 6 and 21 of each course , was mild : only 2 cases of severe leukopenia (< 1500 WBC mm^3) and 1 case with serious infection requiring hospitalization. Eleven pts. (30%) experienced Grade 2-3 WHO stomatitis. Alopecia requiring temporary use of a wig occurred in 14 pts. (38%). No cardiac adverse events were recorded. IVE regimen , even if limited by a short lived response , is an effective combination for salvage treatment of recurrent pretreated MBC . Our results warrant further confirmations in a larger series of patients.

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Mitomycin C, Mitoxantrone and Methotrexate combination (3M) in advanced breast cancer: an effective second line therapy

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3M regimen, originally described by T.J. Powles, is an effective treatment for advanced breast cancer (ABC).In the aim to evaluate tolerability as well as response rates of the above combination when used as a second line therapy, we treated 41 patients (pts) with recurrent ABC with Mitomycin-C: 7 mg/sqm/iv every 6 weeks, Methotrexate: 35 mg/sqm/iv and Mitoxantrone: 7 mg/sqm/iv every 3 weeks until progression or pts refusal. Pretreatment characteristics of patients' sample were: median age 53 (28-71), menopausal status: pre 4 post 36, previous treatment for advanced disease: chemotherapy: 26 (anthracycline containing regiments 20, without anthracyclines 6) endocrine therapy: 26 (MPA 14, TMX 12), dominant metastatic site: visceral 10, bone 11, soft tissue 5, mixed 15, median performance status (KB) 80 (50-100).At Jan. 1993 , a total of 243 courses were administered, the median number of cycles per patient being 6 (2-13). 15 out of 36 fully evaluable patients achieved an objective response (1 CR and 14 PR, 41% - 95% C.I.: 25% - 57%) with a median duration of 10 months (range 5-16). Median time to progression was 8 months. Median survival was 12 months (range 2-20+).
Treatment-related side effects were: leukopenia (20%) thrombocytopenia (4%), nausea and vomiting (19%), mucositis (5%) neuropathy (1pts), hair loss not requiring wig (2pts). No cardiac, renal, pulmonary or liver toxicity were recorded. Drug administration had to be postponed for one week in 48 courses due to myelosuppression.Our results indicate that 3M regimen is an effective and safe second line therapy for advanced, previously treated, breast cancer.

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RESPONSE AND TOXICITY OF TEN DAYS CONTINUOUS INFUSION OF 5-FLUOROURACIL AND INTERMITTENT LEUCOVORIN IN ADVANCED BREAST CANCER.

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No generally accepted standard second line chemotherapy exists after progress on the anthracyclines doxorubicin and farmorubicin in advanced breast cancer. The use of protracted 5-fluorouracil (5-FU) infusion modulated by leucovorin (LV) has gained increasingly interest. Sixteen patients (pts) age 45-78 years with advanced breast cancer and a life expectancy of more than three months have started treatment with 5-FU (250 mg/m^2-day for ten days, Baxter pump + Port-a-Cath) and Leucovorin (LV) (500 mg/m^2-4h days 1,5 and 10) repeated every 29 days. Objective evaluation was performed every third month according to UICC criteria and a life quality questionnaire was answered by the pts every month. All pts had at least one previous chemotherapy treatment for advanced disease and the average number of treatments was 1.8. Of thirteen pts evaluated for response there was 1 CR, 2 PR, 6 NC and 4 PD. The average time on treatment is 6+ months and the average survival from diagnosis of advanced disease is 42 months. The dose-limiting toxicity (WHO criteria) in 80 courses was stomatitis (5 courses grade 3-4, 40 courses grade 1-2) and diarrhea (3 courses 3-4, 13 courses grade 1-2). Other toxicity was nausea/vomiting (1 course grade 3-4, 39 courses grade 1-2), hair loss (4 pts grade 1) and bone marrow suppression (1 course grade 2, 4 courses grade 1). Dose reduction was required in 13/80 cycles. The conclusion is that protracted 5-FU infusion with intermittent LV is active, with tolerable toxicity, in previously treated pts with advanced breast cancer.

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Recurrent metastatic breast cancer treated with high dose Cyclophosphamide (CTX) as 2nd line treatment in a phase II study.

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60 evaluable patients with recurrent breast cancer previously treated with 4-epi-Adriamycin received high dose CTX 2.5 g/m^2 q.3rd weeks as monotherapy. Mesnum was given prophylactic. Dose limiting toxicity was haematologic as 90 percent developed WHO grade 3 - 4 toxicity. Although four patients died in septic leucopenia, the treatment was generally well tolerated. The majority had grade 2 - 3 nausea and vomiting. There was no evidence of haemorrhagic cystitis. The response rate was 32%: 5 patients achieved CR and 14 PR with a median duration of 11 and 5 months, resp., 18 had stable disease - median duration 5 months (2-18) and 23 PD.
In conclusion high dose CTX demonstrates significant activity in patients with advanced cancer mammae. 60% of the responsive patients had recurrence of disease during or within six months from previous treatment with antracyclin indicating that there are no clinical cross resistance.

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VINORELBINE (VNR) IN PRETREATED ADVANCED BREAST CANCER (ABC)

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Scanty data have demonstrated the efficacy of VNR as single agent in ABC. In order to better define the usefulness of this new anticancer agent, we have treated 22 patients with ABC with VNR at the dose of 20 mg/sqm/week without using CSFs. Twenty-one pts were considered evaluable (20 postmenopausal): all had been previously treated with anthracycline and/or mitoxantrone with a median of 4 (3-6) of cytotoxic agents. The median age was 61 (43-73). Dominant sites of disease were: Viscera 10, Bone 9, Soft tissue 17. The median number of lesions was 2 (1-4). The evaluation of response was made after almost 4 doses. The median number of doses administered was 9 (4-17). The median performance status (ECOG) was 1 before and after treatment. The response rate was 47.6% (1CR, 9PR, 5SD, 6PD). The sites of response were Soft tissue 12, Viscera 3, Bone 3. The side effects were: neutropenia 17 pts (GI°8, GII°6, GIII°3), anemia 1, nausea and vomiting 2, constipation 2, local effusion 3, phlebitis 3, alopecia 6.
VNR appears to be a promising agent in the treatment of pretreated ABC and should be tested in combination chemotherapy regimens.

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RAPID DELIVERY OF MULTIPLE COURSES OF HIGH-DOSE CHEMOTHERAPY (HDC) USING G-CSF & PERIPHERAL BLOOD PROGENITORS (PBP) IN PATIENTS (PTS) WITH METASTATIC BREAST CANCER (MBC). Fennelly D, Vahdat L, Hamilton N, Raptis G, Schneider J, Norton L, Crown J. Memorial Sloan-Kettering, NY.
Although single treatments can produce complete remissions (CRs) of lymphomas and other sensitive tumors, cure usually requires multiple cycles. MBC may be similar, but the single treatment which produces 50% CRs in previously untreated disease is HDC, which is not easily recycled. G-CSF allows recycling of cyclophosphamide (C), but not of thiotepa (T) due to its causing thrombocytopenia and cumulative myelosuppression. We applied 2 courses of C (3.0.gm/m^2), then 2 courses of T (500-700 mg/m^2/ course, no intrapatient escalation) by using G-CSF after all courses and harvesting PBP after each C to reinfuse after each T. Pts are discharged from hospital after i.v. PBP, re-admitted for fever or emesis control. 33 pts enrolled, 7 on-study, 1 withdrawal. 3 pts, with heavy prior chemotherapy, had only 1 T course due to PBP collections <0.5 x 10^6/kg/course CD34+ cells. 22 have completed all therapy. Median retreatment interval after C = 14 days; between T doses = 16 days (range 13-22). 1 pt required back-up marrow. Median days after T to neutrophils > 0.5 x 10^9/L = 9 (range 6-36) and platelets > 20 x 10^9/L = 11 (5-36). 40/47 T courses required readmission for fever. There was 1 ocular hemorrhage, 1 reversible neurological toxicity, 3 cases reversible veno-occlusive disease. 5 of 9 evaluable pts in partial response were converted to CR by our HDC. G-CSF plus i.v. PBP permits multiple cycles of HDC, a strategy active against MBC.