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INTENSIVE CHEMOTHERAPY WITH FLUOROURACIL, EPIRUBICIN, CYCLOPHOSPHAMIDE (FEC) DAY 1-8 IN METASTATIC BREAST CANCER.

A Bolognesi, D Aldrighetti, C Verusio, M Ronzoni, G Ceresoli, E Villa.

Department of Radiochemotherapy, S. Raffaele Hospital; Milan, Italy.

From July '89 to September '92 sixty consecutive patients (pts) with metastatic breast cancer have been treated with fluorouracil (F) 500 mg/m2, epirubicin (E) 40 mg/m2, cyclophosphamide (C) 500 mg/m2. All drugs were given i.v. on days 1 and 8 every 4 weeks, without ordinary use of G-CSF. Dose reduction was performed on day 8 in case of incomplete hematological recovery or in presence of grade 4 myelosuppression.
Patients' features were: median age 55 yrs (range 36-73), ECOG P.S. 0-2; 13 pts were previously treated for metastatic disease: 6 with polychemotherapy, 7 with hormonal therapy.
Objective responses were observed in 46/60 pts (76%) with 9 CR (15%) and 37 PR; no PD occurred during treatment; 4/6 pts previously treated with chemotherapy responded to FEC. The optimal planned dose was administered in 22/60 pts (36%); 38/60 pts (64%) had a dose reduction, mainly on day 8; median number of delivered cycles was 6.
Median response duration was 9 mos (range 3-18+) in responders and 6 mos (range 2-12) in NC pts. Median overall survival was 14,5 mos (range 4-36+) for the entire group without difference between RC + RP pts and NC pts.
The main toxicity was hematological; leukopenia grade 3-4 was observed in 65% of pts (13% grade 4); no treatment related deaths were seen; no significant decrease in hemoglobin or platelets count was seen. The other main side effects were alopecia (grade 2-3 in 93%), nausea and vomiting (grade 2-3 in 46%) and mucositis (grade 3 in 7%).
These results suggest that FEC 1-8 is a very active regimen in metastatic breast cancer; it is feasible in output pts with acceptable toxicity. Further studies are needed to determine the optimal duration of chemotherapy and to prolong the duration of response.

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PHASE II TRIAL WITH NAVELBINE (NVB) IN ADVANCED BREAST CANCER (ABC) AS FIRST LINE THERAPY.

J. García-Conde*, A. Lluch*, A. Cervantes*, V. Cervera*, A. Casado*, M. Martín*, E. Díaz-Rubio*, C. Oliveira*, M.H. Gervasio*, J.L. de Pablo*, J.L. García-Girón*, Gorostiaga*, A. Martínez**, F.M. Delgado**.
* Spanish and Portugal Study Group. ** Pierre Fabre Medicament.

From November-89 to June-91, 54 patients with diagnostic of ABC, with measurable disease and previously untreated, were included in a phase II trial receiving a regimen with navelbine (NVB) 30 mg/m^2 weekly. Objective of the study was to confirm previously published dates: Fumoleau and cols (ASCO 1.990 and 13th Annual S. Antonio Breast Cancer Symposium) y Bruno S. and cols. (UICC 15th International Cancer Congress 1.990) who showed more than 40% objetive response rate in ABC with NVB as single agent. Fifty patients, with a median age of 50 years (34-76) and performance status 0-2 (WHO), were eligible and assessable for response and toxicity. 97% were previously treated with surgery, 54% received postoperative radiotherapy and 71% received adjuvant chemotherapy, with more than 12 months of disease free interval. Metastatic sites were: 33% one site, 49% two sites and 18% three or more. Total number of administrated courses was 564 (mean 11 courses). Dose intensity was 68%. Leukopenia grade 3 and 5 were observed in 50% and 6% respectively. Neutropenia grade 3 in 35% and grade 4 in 40% of patients, with 2% who needed hospitalization for fever and severe neutropenia. Gastrointestinal toxicity (nausea and vomiting) was mild or absent. Alopecia grade 2 in 24%. No peripheral neuropathy higher than grade 2 was observed. Overall response rate was 50% (Complete response: 4%, and partial response: 46%). Our dates confirm that NVB has an important activity as single agent in ABC as first line therapy, and it should be included in first line combined regimens of chemotherapy.

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ACTIVITY OF VINORELBINE (VIN) IN ADVANCED BREAST CANCER: PRELIMINARY RESULTS OF A PHASE II TRIAL.

Demicheli R., Terenziani M., Ferrari L., Brambilla C., Moliterni A., Zambetti M., Zucchinelli P., Caraceni A., Martini C. and Bonadonna G. - Division of Medical Oncology, Istituto Nazionale Tumori, Milano, Italy.

From July 1992, 20 patients (pts) with progressive metastatic breast cancer were treated with VIN at a weekly dose of 30 mg/sqm. Median age was 54 years and PS was 90-100. Fifteen pts had been administered prior chemotherapy for metastatic disease or were less than 12 months from the end of adjuvant chemotherapy. Adriamycin and/or CMF had been previously used in 17 pts. So far, 1 CR and 8 PR (SWOG criteria,1992) have been documented in 16 evaluable pts (56% ; 95% c.i.: 30-80%). Main toxic manifestations (20 pts): neutropenia (13 pts grade 3, 5 pts grade 4), local pain (9 pts) and phlebitis (6 pts), fatigue (3 pts grade 2, 2 pts grade 3), fever (11 pts grade 1), nausea (14 pts grade 1-2), hair loss (13 pts) and constipation (7 pts, 2 grade 3). Because of toxicity (mainly neutropenia), 42 % of drug administrations was delayed, and in 7 pts a reduced dose (25 mg/sqm) was administered. Preliminary conclusions: Vinorelbine shows a promising activity in breast cancer, but its schedule needs further refinement.

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CHEMOTHERAPY COMBINED WITH MEDROXY-PROGESTERONE ACETATE IN ADVANCED BREAST CANCER.TWO RANDOMIZED STUDIES.

S.Gundersen,On behalf of The Norwegian Breast Cancer Group.Dept.for Medical Oncology and Radiotherapy,The Norwegian Radium Hospital, 0310 Oslo 3,Norway.

In in vitro studies gestagen (MPA) can render hormone resistant cells more susceptible to chemotherapy (CHT). Patients (138) with estrogen receptor negative advanced disease were therefore randomized between CHT and CHT+MPA - 500mgx2.

The total response rate was 73 % for CHT+MPA vs.46 % for CHT alone (p=0,005).Doses of chemotherapy did not differ.

In a second trial 218 patients that had been treated with and progressed on hormone therapy, including MPA, were randomized. Response rates were 41% versus 30% for CHT alone (p=0,11).

In concordance with experimental studies,there may exist an interaction between CHT and MPA in hormone insensitive metastatic breast cancer.

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ASSESSMENT OF QUALITY OF LIFE DURING SECOND LINE CHEMOTHERAPY FOR ADVANCED BREAST CANCER

E.E. Voest, P.H. Th. Slee, H. de Haes, S.G.L. van der Vegt, and J.W.R. Nortier.
St. Antonius Hospital Nieuwegein, Oudenrijn Hospital Utrecht and Diakonessen Hospital Utrecht, Departments of Internal Medicine and Oncology, The Netherlands.

Objective. The aim of this study was to evaluate changes in quality of life (QoL) after second line chemotherapy for advanced breast cancer. Methods. Twenty-nine women with advanced breast cancer, relapsed after CMF (cyclophosphamide, methotrexate, fluorouracil), were randomised to receive either weekly epirubicin (25 mg/m^2, 15 patients) or three weekly mitoxantrone (14 mg/m^2, 14 patients). The Rotterdam symptom check list (RSCL) was used to score QoL and was mailed to the subjects before, and 6, 9, and 12 weeks after the start of treatment. The forms were returned by mail to an independent investigator. Results. Due to rapid progression within the first 6 weeks of treatment 6 women were excluded for assessment of QoL. Survival after start of treatment was short (8,9 and 7.8 months for epirubicin and mitoxantrone treatment respectively). Besides one partial remission in the epirubicin arm no further objective remissions were achieved. Mitoxantrone did not improve nor impaire the psychological or physical condition (n=10) in comparison with the pretreatment condition. Epirubicin (n=13) significantly (p=0.032) impaired the physical condition whereas the mental status remained unaffected. Conclusion. Although the deterioration of QoL due to the natural course of the disease was not evaluated in this study it appears that second line chemotherapy offers very little benefit in improving QoL. If second line chemotherapy for advanced breast cancer is considered patients may best be entered in a trial evaluating novel anti-cancer drugs.

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MITOXANTRONE AND VINORELBINE IN SALVAGE CHEMOTHERAPY OF ANTHRACYCLINE-REFRACTORY ADVANCED BREAST CANCER

P. Silvestro, G. Caparrotti, G.S. Bruni, E. Ferrari, P.G. Maida, M. Coscione, G. Caliento, L. De Rosa, M. Pergola
Division of Medical Oncology B, National Cancer Institute, Napoli, Italy.

Mitoxantrone and vinorelbine are active drugs in advanced breast cancer. Patients (pts.) who had previously shown disease progression as they were treated with doxorubicin or epirubicin, received mitoxantrone at a dose of 12 mg/m2 i.v. on day 1 and vinorelbine at a dose of 25 mg/m2 i.v. on day 1 and 8; cycles were repeated every 3 weeks. Characteristics of 10 evaluable pts.: median age 56 years, performance status (ECOG) <2, premenopausal 2 pts., postmenopausal 8 pts., estrogen receptors positive in 5 pts., negative in 3 pts.; dominant metastatic sites were bone 4 pts., viscera 4 pts., soft tissues and lymph nodes 2 pts. In 7 pts. mitoxantrone and vinorelbine was given as second line and in 3 pts. as third line. Preliminary results (WHO): 4/10 (40%) partial responses, 3/10 (30%) stable diseases, 3/10 (30%) progessive diseases. Nausea, vomiting and loss of hair were moderate or absent; leukopenia grade 3-4 occurred in 3 pts.; no cardiotoxicity was observed.