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CONTINUOUS IV INFUSION OF VINORELBINE (VNB) AND BOLUS CISPLATINUM (CDDP) (CIVIC REGIMEN) AN EFFICIENT REGIMEN IN HORMONO RESISTANT METASTATIC BREAST CANCER (MBC), AFTER FAILURE OF ANTRACYCLINE AND/OR PACLITAXEL

I. Ray-Coquard, J.Y. Blay, T. Bachelot, D. Berton, J.P. Guastalla, G. Catimel, T. Philip, P. Rebattu, J.P. Droz, P. Biron
Centre Léon Bérard, 28, rue Laënnec, 69373 Lyon Cedex 136, France

We have investigated a new chemotherapy regimen (CT) in patients (pts) previously treated with CT and/or hormonotherapy. CDDP of 20 mg/m^2/day was given, (D1 to D5) every 21 days in 1 H iv infusion and VNB was given with the dose of 6 mg IVD bolus, followed by VNB 6 mg/^{2}/day in continuous iv infusion (D1 to D5) every 21 days. 59 pts were included in this trial (median age: 46 years, range 28–49; premenopausal: 40 pts). Respectively 44 and 12 pts had previously anthracyclines (adm) and paclitaxel containing regimens. Overall 212 courses were given (median 3, range 1–6): myelosuppression was the most frequent side effect: neutropenia WHO grade III occurred in 41 courses (20%) on 212 and grade IV for 64 courses (31%). Thrombopenia WHO grade III and IV for 23 courses (12%). No cumulative toxicity was observed on bone marrow. Grade II peripheric neuropathy was observed in 12 of 212 courses (6%) and grade III in 4 of 212 courses (2%) with correlation between toxicity and numbers of courses. Neuropathy (grades II and III) occurred most often after 4 courses (CHI 2: 30.2; $P < 0.001$). Nausea and vomiting: grade II and III in 106 courses (50%). 56 pts were evaluable for response: CR-PR (complete response-partial response: objective response) in 24 pts (43%) (95% ci 23–63%), CR rate was 4%, MR-SD (minimal response-stable disease) in 24 pts (43%). The median time for response was 10 weeks. The median duration of response was 18 weeks. Response by sites: 16 CR-PR in 37 responses for pulmonary site (44%); 8 CR-PR in 18 for cutaneous site (45%); 19 CR-PR in 48 for hepatic (40%); 18 CR-PR in 49 for bone (37%). Response rate after the 2 first courses was 41% in ADM resistant and 58% in ADM + paclitaxel resistant pts.

CIVIC is an effective and well tolerated regimen in MBC resistant to previous anthracylines and/or paclitaxel containing CT.

A number of 4 courses seems to give the best toxicity-efficacy ratio.

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TAXOL® (PACLITAXEL) 225 MG/M^2 BY 3-HOUR INFUSION WITHOUT G-CSF AS A FIRST LINE THERAPY IN PATIENTS WITH METASTATIC BREAST CANCER (MBC)

J. Bonneterre[1], M. Tubiana-Hulin[1], Ph. Chollet[1], B. Chevallier[1], P. Fumoleau[1], P. Kerbrat[1], B. Vié[1], D. Khayat[1], N. Tubiana[1], C. Lejeune[1], A. Le Grand[2], J.A. Soares[2], B. Pellae-Cosset[2]
[1]Breast Cancer French Study Group, France
[2]Bristol-Myers Squibb, France

A hundred twenty-one patients (pts) were included in a phase II trial of Taxol (T) 225 mg/m^2 by 3-h infusion q3w, without G-CSF, as 1st line treatment for MBC. We report here the preliminary results on the first 50 pts. Eligibility criteria were: age 18–75, ECOG PS $\leqslant 2$, measurable disease, disease-free interval $\geqslant 12$ months and adequate organ function. Pts characteristics were: median(med) age 51 years (range 27–71); med ECOG PS 0 (0–2); 23 pts received prior neoadjuvant/adjuvant CT and 27 pts received no prior CT. A total of 297 cycles have been administered with a med number of T courses/pt of 6 (1–12). All pts are evaluable for toxicity and 47 for efficacy.

Grade III/IV neutropenia was seen in 27% cycles with febrile neutropenia in only 3 courses (1%). Treatment was never delayed because of slow hematologic recovery. Peripheral neuropathy grade $\geqslant$ II was noted in 25 pts: 18 (36%) grade II and 7 (14%) grade III. The med cumulative dose of T at appearance of grade III neurotoxicity was 1125 mg/m^2 (675–2475).

There were 4 CR, 17 PR, 12 SD and 14 PD for an objective response rate of 45%.

Conclusion: These preliminary results confirm that Taxol is a very active drug as a first-line therapy for MBC. It can be administered as a 3-hour infusion at a dose of 225 mg/m^2 q3w with an acceptable safety profile.

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A RANDOMIZED PILOT CLINICAL TRIAL COMPARING 5 VERSUS 10 μG/KG FILGRASTIM (NEUPOGEN) AFTER FEC CHEMOTHERAPY IN ORDER TO COLLECT PERIPHERAL BLOOD STEM CELLS (PBSC)

L. D'Hondt, M. André, Th. Guillaume, A.M. Feyens, J.L. Canon, Ch. Doyen, Y. Humblet, J. Longueville, H. Vannerom[1], M. Symann
Groupe d'Oncologie de l'Université Catholique de Louvain, 1200 Brussels
[1]Amgen Belgium

Chemotherapy followed by hematopoietic growth factor (HGF) is a effective way to collect PBSC. The optimal dose of HGF for mobilizing PBSC is not yet known. We conducted a randomized pilot clinical trial comparing two doses of filgrastim administered after FEC chemotherapy in breast cancer patients (pts). Sixteen pts were randomized to receive either 5 (group I) or 10 (group II) μg/kg filgrastim (Neupogen, Amgen). Eight pts were enrolled in each arm. FEC chemotherapy combined 5-FU, epirubicin, and cyclophosphamide. Filgrastim was administered daily subcutaneously until the second day of leukapheresis. Three Leukaphereses were performed. Pts characteristics were comparable in the 2 groups. Thirteen pts were fully evaluable; 7 in group I and 6 in group II. Total numbers of CD34 + cells collected after 3 leukaphereses were significantly greater in group II than in group I: 4.26 10^6/kg (9–81 10^6) versus 1.377 10^6/kg (0.3–5.3 10^6) $P < 0.05$. All but one pts were autografted after high dose chemotherapy (STAMP V). No difference was seen between the two groups in term of hematologic recovery. We can conclude that it seems to exist a dose-dependent effect of filgrastim for mobilizing PBSC. Ten ug/kg after FEC chemotherapy allow to collect significantly more CD34+ cells than 5. No advantage in term of hematologic recovery is observed.

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A RANDOMISED, DOUBLE-BLIND, MULTICENTRE CROSSOVER TRIAL TO EVALUATE *IN-VIVO* INHIBITION OF AROMATASE BY ARIMIDEX (ZD1033) (1 MG AND 10 MG PO OD) IN POSTMENOPAUSAL WOMEN WITH BREAST CANCER

M. Dowsett[1], N. King[1], P.E. Lønning[2], J. Geisler[2], P.O. Kormeset[3], P.L. Walton[3]
[1]Royal Marsden NHS Trust, London, U.K.
[2]Haukeland Hospital, Bergen, Norway
[3]ZENECA Pharmaceuticals, Macclesfield, U.K.

ARIMIDEX (A) is a new aromatase inhibitor which has been shown to be a potent and highly selective in Phase I studies. It has also been evaluated in multicentre studies in the US and Europe for comparative clinical efficacy against megestrol acetate in postmenopausal women with advanced breast cancer.

In this study we have compared the effect of once daily orally administered A (1 and 10 mg) on whole body aromatisation in 10 pts with breast cancer using a modification of the method described by Jacobs et al. (1991). A was well tolerated at both doses.

Whole body aromatase was reduced by approx 95% after 28 days of treatment with either dose of A and the plasma concentration of oestrone, oestrone sulphate and oestradiol by >80; >90 and >80% respectively. Whereas the levels of AD showed no consistent change.

These data indicate that 1 mg OD PO of A can maximally inhibit aromatisation in pts and that this is associated with a profound decrease in circulating estrogens.

Jacobs S *et al.* Journal of enzyme inhibition 4:315–325 (1991)

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LONG-TERM SURVIVORS AFTER HORMONOTHERAPY (HT) IN METASTATIC BREAST CANCER (MBC). A RETROSPECTIVE STUDY

B. Esteban, J.A. Arranz, V. Alija, C. López, M. Erustes, M. Feyjoo, P. López, A. Alonso, G. Pérez Manga
Serv. de Oncologia Médica, Hosp. Gen. Univ. Gregorio Marañón, Madrid, Spain

From a data base of 1724 patients (p) with MBC, we have analyzed a group of 436 p (25.3%) treated with HT as single first-line treatment. Patients who received simultaneous local therapy or chemotherapy were excluded. Treatment was elected according to clinical criteria.

Pretreatment characteristics: Mean age was 57 years (26–88), 429 p (98.4%) were female and 50% underwent adjuvant treatment of the primary tumor (median disease free interval: 24 months (m), range 0–276). Eighty-three percent (356 p) had suppressed ovarian function at the time of metastatic disease. One single metastatic site was seen in 66% of p.