375 POSTER

EFFECT OF ADJUVANT CHEMOTHERAPY (ACT) WITH OR WITHOUT ANTHRACYCLINES ON FIRST LINE CEF IN METASTATIC BREAST CANCER PATIENTS (PTS)

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The effect of previous ACT with or without anthracyclines on the overall survival (OS), progression free survival (PFS) and response rate (RR) was evaluated in 326 metastatic breast cancer pts entered into 4 consecutive randomized trials and treated with CEF (Cyclophosphamide, Epidoxorubicin, 5-Fluorouracil) as first line CT. 154 (44%) pts did not receive previous ACT, 143 (44%) and 39 (12%) pts received CMF-based and anthracycline-based ACT, respectively. Response to CEF was observed in 161 (49.4%) pts. At univariate analysis, pts who received prior ACT had a significantly lower probability of response than pts who did not: 43% versus 58% ($P = 0.02$). No difference between CMF-based (RR 43%) and anthracycline-based (RR 44%) ACT was observed. Stepwise logistic regression analysis indicated that ACT, metastatic site and previous hormonotherapy for metastatic disease, were the most important factors in predicting the RR. At the multivariate analysis ACT was one of the strongest factor associated with a poor PFS. Median OS was 17.9 months. Pts who did not receive ACT had a longer survival (21.1 months) compared to pts previously treated with CMF-based (15.3 months) or anthracycline-based (15.8 months) ACT. Previous ACT adversely affects RR, PFS and OS in metastatic breast cancer pts treated with CEF regimen as first line chemothorapy. No difference between pts previously treated with CMF-based or anthracycline-based ACT was observed.

376 PUBLICATION

ORAL DOXIFLURIDINE PLUS LEUCOVORIN IN ELDERLY PATIENTS WITH ADVANCED BREAST CANCER

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In an ongoing phase II study, 37 elderly patients (≥70 year) have been treated with oral doxifluridine 600 mg/m^2 plus oral l-leucovorin 25 mg, both q 12 hours days 1–4. The courses are repeated every 12 days. A total of 230 courses have been given, with a median of 4 cycles per patient (range 1–14). The main patient characteristics are a median age of 76 years (range 70–88), median ECOG performance status 0 (range 0–2), soft tissue, viscera and bone involvement in respectively 81%, 46% and 27% of patients. Seventeen of the 37 patients have previously received chemo and/or hormonotherapy for metastatic disease.

The grade 1–2 (NCI) side effects are: nausea and vomiting (37%), diarrhea (26%), mucositis (14%), gastric pain (3%), leukopenia (11%), piastrinopenia (9%), anemia (9%). Grade 3 nausea and vomiting has been observed in 1 patient and grade 3 diarrhea in 4 patients. Only 1 patient has experienced grnde 4 diarrhea.

In the 32 evaluable patients, 1 CR, 8 PR (CR + PR = 28%, C.I. 95% = 28 ± 15), 11 SD and 12 PD have been recorded. The 17 previously untreated patients show a response rate of 35% (1 CR + 5 PR) with a median response duration of 4 months (1+ – 15+); the 15 pretreated patients include 3 PR (20%) with a median duration of 2 months (1+ – 4). Doxifluridine plus l-leucovorin is a treatment with promising activity and good compliance when delivered in an out-patient setting.

Data management by ITMO (Italian Trials in Medical Oncology) Scientific Service.

377 PUBLICATION

THERAPEUTIC EFFECTS OF THE AROMATASE INHIBITOR FADROZOLE (F) HYDROCHLORIDE IN ADVANCED BREAST CANCER

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In order to determine the endocrine effects and evaluate tumour response of the 3 doses of fadrozole (F), a new potent oral non-steroidal aromatase inhibitor, a multi-centre randomised double-blind study has been performed in post-menopausal (PM) patients (pts) with recurrent breast cancer after tamoxifen failure. Treatment allocation was randomly 0.5, 1.0 or 2.0 mg orally bd. Toxicity was assessed using WHO criteria and the response was assessed using UICC criteria. The endocrine component of the trial lasted for 3 months. 80 pts were entered on study. 8 are not assessable for toxicity or response; 3 have no measurable or evaluable disease, 2 received trial treatment for less than 27 days due to disease-progression, 1 stopped trial treatment after 6 days due to disease-progression, 1 was lost to follow-up and 1 had hypercalcaemia the day after the start of trial. In general the pt characteristics (dose of F, age, disease-free interval, performance status, menopausal status, years PM, ER status, metastatic sites, dominant site of metastatic disease and previous treatment for metastatic disease) were well balanced between the 3 randomised groups. We have previously reported that F achieves near maximal suppression of oestrogen at 1 mg bd. The objective response rate (RR) was 17% (95% CI: 8.9–27.3%) with no complete responders. 15 pts (21%) had stable disease (NC) and 45 pts (63%) had progressive disease (PD). There was no significant difference in the RR between pts receiving 0.5 mg, 1 mg and 2 mg of F bd. The median duration of objective response was 36 weeks (wks). The median time to treatment failure was 12.7 wks. The log rank test showed no statistical difference between the dosage groups. The main adverse events reported were of mild to moderate severity; nausea in 11 pts (15%), hot flushes in 4 (5%) and somnolence in 3 (4%). 2 pts stopped therapy because of side-effects (somnolence, depression) but the causal relationship remained uncertain. No serious adverse events were reported. In conclusion F is a clinically active aromatase inhibitor with a low incidence of side-effects and phase III clinical trials in PM patients are currently underway.

378 PUBLICATION

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

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We report the preliminary results on 50 out of 86 pts enrolled to an ongoing trial of Taxol (T) as 2nd line treatment for MBC. T dose is 225 mg/m^2 (3-h infusion) q3w without G-CSF. Eligibility criteria: age 18–75. ECOG PS ≤ 2, measurable disease and adequate organ function. Pts characteristics are: median (med) age 55 (range 36–76); med ECOG PS 1 (0–2); 24 pts received prior adjuvant + metastatic CT (group A) and 26 pts received only 1 prior metastatic CT (group B). Patients received a total of 217 cycles with a med number of T courses/pt of 4 (1–11). Fourty-nine pts are evaluable for toxicity and 46 for efficacy.

Grade III/IV neutropenia was observed in 58% cycles. Febrile neutropenia was reported in only 3% cycles and grade III anemia in 5% cycles. No thrombocytopenia grade ≥ 3 was reported. Peripheral neuropathy grade ≥ 2 was noted in 31 pts: 20 (41%) grade II and 11 (22%) grade III. The med cumulative dose of T at appearance of grade III neuropathy was 900 mg/m^2 (450–1350). There were 2 CR, 11 PR, 22 SD and 11 PD, for an objective response rate of 28% (group A: 15%; group B: 38%).

Conclusion: Taxol 225 mg/m^2 as a 3-h infusion is a safe schedule for 2nd line pts with MBC. These preliminary results suggest an encouraging efficacy in this setting.

379 PUBLICATION

L-FOLINIC ACID (FA), FLUOROURACIL (FU), ESCALATING DOSES OF MITOXANTRONE (N), CICLOPHOSPHAMIDE (C) AND G-CSF IN ADVANCED BREAST CANCER PATIENTS (ABC). A PHASE II STUDY

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In order to verify if an increased dose intensity is associated with higher response rate and improved survival, starting from September 1993 untreated patients (pts) with ABC were enrolled in a multicentric study of GOIM (prot. n 9304). Chemotherapy consisted (mg/mq) of L-FA 100 iv d 1–3, F 340 iv d 1–3, N 12 iv d 1 and C 600 iv d 1. G-CSF was administered sc at 0.5 μgr/kg from day 5 to 14. Mitoxantrone was escalated by one dose level (2 mg/mg) up to a maximum of 18 mg/mq according to nadir toxicities. Treatment was repeated every 3 weeks or was moved up