1321 PUBLICATION

Palliative chemotherapy with escalated single Ifosfamide dose in an ambulatory setting for patients with advanced breast cancer

S. Reyes[1], J. Cuevas[1], D. Román[1], G. Rodríguez[1], R. Fernández[1], S. Cervantes[1], L. Torrecillas[2]. [1]*Grupo Oncologico Cooperativo Del Centro De Mexico, GOCCEM;* [2]*CMN 20 Noviembre ISSSTE, Mexico*

Ifosfamide has single drug activity of 47% in advanced breast cancer (ABC). For other tumors, a dose-dependent response rate is known. Data regarding the best monosubstance level for ABC is absent. Since Feb. 97, 28 pts with ABC, naive to palliative chemotherapy, received ambulatory Ifosfamide: starting dose 2.5–3 g/m^2 days 1–3 every 21 days. Dose was escalated for the following cycles 20%, if hematological toxicity and general tolerance were less than G-3. Mesna: i.v. 500–600 mg/m^2 at hour 0 + 4 and 1000–1200 mg/m^2 po at hr 8 + 14. Patients (pts): mean age 49 years old (24–63 y); stage IV 18 pts, relapse 9 pts, persistent IIIB one pt; site of metastasis: lymph node 19, bone 18, breast 17, lung 10, skin 4, liver 2, pleural, mediastinum and eye one each; performance status: mean ECOG 1; median DFI = 13.2 months.

Results: PR 20/28 pts (71%), SD 1 pt (4%) and Progression 7 pts (25%); 3 PR and 1 SD still under treatment. Subjective symptoms improvement when applicable: yes = 18 pts, no = 5 pts; number of Ifosfamide delivered cycles = 4.4 (1–6); maximal known response to Ifosfamide: at 1st cycle = 16 pts, 2nd = 2 pts, 3rd = 1 pt. Dose escalation possible in 22 pts, not performed in 6 pts (2: intolerance, one: omission, 3: progression). Escalation was possible at least to 9 g/m^2 per cycle and some cases even to 11.5, 12 and 15 g/m^2 without G-CSF. Non hematological toxicity: G-3 cystitis 1 pt; G-3 emesis 3 pts, mild muscular pain 10 pts; dizziness 4 pts; mesna oral taste intolerance 3 pts; unexplained oedema 2 pts.

Conclusions: 1. Ambulatory high dose Ifosfamide monotherapy is feasible, with OR of 71% 2. Response rate shows to be early (65% at 1–2 cycle) and symptoms relief good: 18/23 pts. 3. Escalation at least to 9 g/m^2 was feasible and safe in 22/25 pts. As a single drug, Ifosfamide has a related dose-response in ABC. Combination with other drugs, deserve Ifosfamide dose level maintenance.

1322 PUBLICATION

Immunologic approaches for breast cancer patients in the setting of stem cell transplantation

R. Ben-Yosef[1], R. Or[1], E. Naparstek[1], G. Varadi[1], A. Ackerstein[1], S. Slavin[1], A. Nagler[1]. [1]*Hadassah-Hebrew University Hospital, BMT, Jerusalem, Israel*

As cure rate in breast cancer (BC) is still limited there is a need for new therapeutic approaches. We have previously demonstrated improved survival and disease free survival in patients with leukemia and lymphoma by using immunologic approaches including cytokines, growth factors and donor lymphocyte infusions post autologous stem cell transplantation (ASCT). We therefore hypothesized that this approach may be of value for patients with BC. Twelve BC pts received s.c. rhGM-CSF (2.5 mcg/kg) X3/w for 3 months post ASCT (group 1) as rhGM-CSF have been shown to potentiate anti BC tumorogenicity in both cell line and animal models through activation of monocytes, dendritic cells, TNF production and antigen presentation. Twelve other patients served as control (group 2) and received GM-CSF for a short period (up to engraftement). Seven other patients were treated with allogeneic stem cell therapy (group 3). The conditioning regimen included carbopatin, thiotepa, etoposide and melphalan for group's 1 + 2 and cyclophosphamide/fludarabine and ATG for group 3. GM-CSF administration resulted in moderate toxicity including fever and rash in 4 patients both in the study and the control groups. No difference in survival and disease free survival was observed in group 1 and 2. Out of 7 patients that received allogeneic cell therapy 5 patients developed graft versus host disease. In summary cytokines and cell mediated immunotherapy should be further evaluated in breast cancer patients as attempts to improve therapeutic options in this cohort of patients are mandatory.

1323 PUBLICATION

Vinorelbine and farmorubicin as neoadjuvant chemotherapy in locally advanced breast cancer

R.M. Gaafar[1], M.R. Hamza[1], H. ElZawahry[1], H. Khaled[1], A. Helal[1], S. Eissa[2], H. AbdelBaki[3], M. ElKalaawy[4]. [1]*NCI, Medical Onc., Cairo;* [2]*NCI, Pathology, Cairo;* [3]*NCI, Radiotherapy, Cairo;* [4]*NCI, Surgery, Cairo, Egypt*

Purpose: The combination of vinorelbine and farmorubicin proved to be highly effective in metastatic breast cancer. In a prospective study, we evaluated vinorelbine and farmorubicin as neoadjuvant chemotherapy (NCT) in stage 3 A and B breast cancer.

Patients and Methods: Between March 1997 and March 1999, 53 consecutive patients with locally advanced breast cancer were entered into the trial. The median age was 37 (24–66 years), median tumor size was 8 cm. Patients were submitted to 3 cycles of NCT. The regimen consisted of vinorelbine (25 mg/m^2 IV infusion d 1 and 5), and farmorubicin (40 mg/m^2 IV d1 and 5) every 21 days. Patients were then submitted to modified radical mastectomy followed by ER (45 cGy/4 weeks). The treatment was completed by another 3 cycles of chemotherapy followed by tamoxifen in cases having tumors with positive hormone receptors.

Results: After a median follow up of 8 months, 3/53 (5.5%) achieved CR and 45/53 (85%) patients had PR. Two patients had SD (3.8%) while 3 cases (5.7%) had PD. Following Chemotherapy, 38 cases (72%) were subjected to Surgery. Patients received 232 cycles, the median number of courses per patient was 5 (range 2–6). Up till now, 11 patients (21%) relapsed. Toxicity: Leucopenia grade 3 and 4 was encountered in 15 cases (28%), alopecia in 50 cases (94%), Phlebitis in 35/53 (66%) and neurotoxicity in 20 cases (38%).

Conclusion: The combination of vinorelbine and farmorubicin is an effective regimen when used as NCT in locally advanced breast cancer with acceptable toxicity.

1324 PUBLICATION

Taxotere® (T) and doxorubicin (D) combination: A phase II South American study in first line treatment (tt) of metastatic breast cancer (MBC)

C. Vallejos[1], P. Nunez[2], L. Orlandi[3], H. Carranza[4], M. Fodor[3], J.M. Reyes[3], A. Majlis[3], P. Gavilanes[5], B. Boussard, E. Salas[6]. [1], *Peru;* [2], *Venezuela;* [3], *Chile;* [4], *Colombia;* [5], *Ecuador;* [6], *Mexico*

T and D are the most active single agents used in the tt of MBC. D has long been considered as a standard and T has demonstrated a superior antitumor activity in a phase III trial (Chan et al., SABCS 97). When combined, high response rates have been observed. A confirmatory phase II study was undertaken in Chili, Colombia, Ecuador, Peru, Mexico and Venezuela. D was administered at 50 mg/m^2 (d 1 i.v. bolus) followed 1 hour later by T 75 mg/m^2 q 3 wks for 6 cycles followed, for responders, by 3 cycles of T alone at 100 mg/m^2. 3 days oral premedication with 8 mg bid dexamethasone was given. The main eligibility criteria were: proven locally advanced or MBC, age < 65, PS ≤ 2, no prior chemotherapy (CT). For adjuvant or neoadjuvant at least 12 months interval between the end of CT and first relapse. 80 pts have been treated and the results are presented on 33 pts. The main characteristics are: median age 48 years (26–65), 94% PS 0–1, median organ involved 2 (1–6), 52% with visceral involvement, 187 cycles have been administered with 186 at full dose. Preliminary overall RR is 69.6% with 13% of complete response. Neutropenia (per pt) grade 3/4: 75%, febrile neutropenia 18%, 6% of cycle. No G 3/4 infection has been reported. Full data will be presented at the meeting.

1325 PUBLICATION

A phase I study of docetaxel (D) in combination with high dose cyclophosphamide (C) as first line chemotherapy in patients (pts) with metastatic breast carcinoma (MBC)

C. Cuvier[1], G. Romieux[2], S. Culine[2], C. Boccara[3], M. Espié, P. Cottu[1], M. Marty[1]. [1]*Hôpital St Louis, Paris;* [2]*Centre Val d'Aurelle, Montpellier;* [3]*Laboratoires Rhône-Poulenc Rorer, Montrouge, France*

There is a need for development of combination of new drugs such as D with non-anthracycline classical ones such as C. This ongoing study explores the feasibility of DC combination administered every 2 weeks in previously untreated pts for MBC, without G-CSF prophylactic support. Eligible pts have a progressive MBC, no prior chemotherapy for metastatic disease, no prior taxanes, age ≥ 18 and ≤ 65 years, WHO PS ≤ 2. To date, 35 pts have