362 Poster

Phase II trial with letrozole (2.5 mg) to maximal response as neoadjuvant endocrine therapy in postmenopausal patients with ER/PgR[+] operable breast cancer

A. Llombart[1], A. Galán[2], C. Fuster[1], E. Buch[2], V. Carañana[3], A. Rodríguez-Lescure[4], C. Vázquez[1], A. Guerrero[1], A. Ruiz[1], V. Guillam-Porta[1]. [1]*Instituto Valenciano de Oncología, Servicio de Oncología Médica, Valencia, Spain;* [2]*Hospital de Sagunto, Servicio de Oncología Médica, Valencia, Spain;* [3]*Hospital Arnau de Vilanova, Servicio de Oncología Médica, Valencia, Spain;* [4]*Hospital Universitario de Elche, Servicio de Oncología Médica, Alicante, Spain*

Background: Randomized trials in postmenopausal patients with ER/PgR[+] operable breast cancer had shown that neoadjuvant therapy with an aromatase inhibitor (AI) is more effective than tamoxifen and equivalent to chemotherapy in terms of ORR and preserving breast surgery. However, trials were conducted with a predetermined length of 3 to 4 months of therpy, and no study has analyzed as yet the optimal duration of AI as induction therapy. In this study we assessed the safety and efficacy for letrozole (Femara®), in postmenopausal women with ER and/or PgR[+] until maximal response.

Material and Methods: An open, multicentric, phase II trial to evaluate the efficacy of letrozole over a preoperative period of 3 months to 1 year was conducted. Inclusion criteria required: Postmenopausal status, histological diagnosis (tru-cut) of infiltrating breast carcinoma, ER and/or PgR[+] (by IHC), tumor stage II to IIIb (T2>2 cm,T3,T4b, N0–2,M0) non suitable for conservative surgery. Inflammatory or T4a tumors were excluded. The primary endpoint was to determine the median duration of treatment to optimal response defined as the interval of time required to achieve the maximal response by clinical exam. The ratio of clinical responses and the frequency of conservative surgery were secondary objectives.

Results: Seventy patients have been recruited in four centers from June 2003 to September 2005. This report includes a preliminary efficacy analysis with the first 30 patients. Median age: 79.8 years (68–91). Stage T2 N0 (59.1%), ER[+] (95.4%). No severe adverse event was reported, and only minor muscle-esqueletal symptoms were noted. The median time to objective and to maximal response were 3.5 months (2.3–4.7) and 4.2 months (4.0–4.4) respectively. At the time of maximal response, the ORR was 80.0%; 53.3% obtaining a PR and 26.7% a CR.

Conclusions: Letrozole shows a high activity and tolerability as neoadjuvant endocrine therapy in elderly patients with endocrine dependent criteria breast cancer. Mature results with the optimal duration of this approach will be helpful to increase local disease control.

363 Poster

Reinduction chemotherapy in T4 breast cancer high risk patients who failed achieving pCR after primary chemotherapy: 6 years survival in a pilot Italian study (ICARO 1)

M.T. Ionta[1], A. Scanu[1], A. Carta[1], D. Vacca[1], A. Contu[2], A. Farris[3], A. Catino[4], S. Palmeri[5], L. Minerba[6], B. Massidda[1]. [1]*University of Cagliari, Medical Oncology, Cagliari, Italy;* [2]*General Hospital, Medical Oncology, Sassari, Italy;* [3]*University of Sassari, Medical Oncology, Sassari, Italy;* [4]*Cancer Institute, Medical Oncology, Bari, Italy;* [5]*University of Palermo, Medical Oncology, Palermo, Italy;* [6]*University of Cagliari, Statistical Unit, Cagliari, Italy*

Background: Locally advanced breast cancer (LABC) is an heterogeneous group of tumors including T4 abc and T4d who are known to have an aggressive clinical course, resulting in early recurrence and death. In spite of improvement in treatment approach the prognosis remains dismal in most patients. Pathological Complete Response after primary chemotherapy both in breast and in axilla (pCR), is the main determinant for better DFS and OS. Viceversa the lack of pathological complete response in breast or in axilla (<pCR) identifies patients who have higher risk of early recurrence and death in spite of the standard neoadjuvant and post surgical chemotherapy and radiotherapy.

Purpose: The aim of our study was to evaluate the impact on further chemotherapy courses on DFS and OS after adjuvant therapy in the <pCRs.

Patients and Methods: From September 1998 to November 2001, 48 consecutive T4 patients (75% T4 abc; 25% T4 d; 88% clinical nodes involvement) median age 51 (29–70) were treated by a multimodality approach with 6 courses of intensive primary PEV regimen (Cisplatin 50 mg/m^2; Epirubicin 100 mg/m^2; Vinorelbine 25 mg/m^2) every 14 days + G-CSF, followed by surgery, radiation, adjuvant CMFx6 and hormone therapy. After adjuvant CMF, patients with <pCR in surgical specimen (35 pts) were randomized 4: 1 to receive observation (28 pts, pLN+ 68%;T4d 21%) (OBSERVATION) or a reinduction chemotherapy (7 pts, pLN+ 71%;T4d 43%) with Epirubicin 100 mg/m^2 q21 x 3 followed by Docetaxel 100 mg/m^2 q21 x 3 (REINDUCTION).

Results: At a median follow-up of 72 months (46–84), 6 years DFS and OS in the pCR group were 92% and 92% respectively. Among the patients in the <pCRs, 6 years DFS and OS in the REINDUCTION group were 100% and 100% respectively; 6 years DFS and OS in the OBSERVATION group were 53% and 68% respectively.

	DFS			OS		
<pCR (35 pts)	Overall	T4 d	pLN+	Overall	T4 d	pLN+
Observation (28)	53%	50%	48%	68%	50%	63%
Reinduction (7)	100%	100%	100%	100%	100%	100%

Conclusions: Reinduction chemotherapy is an effective option in<pCRs, special in very high risk patients as T4 d and pLN + after primary chemotherapy.

These suggestive findings prompt us to design a prospective multicenter randomized phase III study (ICARO 2).

364 Poster

Capecitabine as adjuvant therapy for elderly breast cancer (BC) patients (pts): a pilot study

C. Bernard-Marty[1], G. Demonty[1], N. Personeni[1], G. Ismael[1], F. Cardoso[1], E. Kabanga[1], A. Bexon[2], J. Nogaret[1], L. Biganzoli[3], M. Piccart[1]. [1]*Jules Bordet Institute, Medical Oncology Clinic, Brussels, Belgium;* [2]*Hoffmann-La Roche, Nutley, USA;* [3]*Jules Bordet Institute, Medical Oncology Clinic, Brussels, Belgium;* [3]*Prato Hospital, Department of Oncology, Prato, Italy*

Background: The benefit:risk ratio of adjuvant chemotherapy (CT) remains debatable for elderly pts with BC. Capecitabine (Xeloda®) (X) is an active and well-tolerated treatment for elderly pts with metastatic BC. The current trial has been designed to determine the feasibility of delivering 6 cycles of X as adjuvant CT in high risk BC pts ⩾70 years old. Objectives were to determine the rate of pts receiving an acceptable relative dose intensity (RDI), while experiencing acceptable side effects.

Patients and Methods: Eligibility criteria for study participation were age ⩾70 years old and histologically proven BC. High risk BC was defined as endocrine non-responsive (ER– *and* PgR–) *or* endocrine responsiveness doubtful (ER and/or PgR– or poor) and other risk factors (pT ⩾2 cm, N+, grade 3 or HER 2+) *or* endocrine responsive (ER+ *and* PgR+) and ⩾2 risk factors *or* very high risk (N ⩾ 4) with any ER/PgR. The planned treatment was 6 cycles of oral X 1000 mg/m^2 twice daily on days 1–14 every 3 weeks, unless severe toxicity developed. A full comprehensive geriatric assessment (CGA) was performed at baseline and after completion of CT.

Results: Between 01/2003 and 07/2005, 29 pts were enrolled. Baseline characteristics: mean age 74.9 (range 70–80); performance status (PS) 0: 81%, PS 1: 19%; infiltrating ductal carcinoma 74%; mean size 3.04 cm (range 0.8–6.7); grade 3: 56%; N 0: 45%, N 1–3: 30%, N ⩾ 4: 25%; ER– and PgR–: 45%, ER– or PgR–: 30%, ER+ and PR+: 25%; HER2+ (3+ by IHC or confirmed by FISH): 15%. Regarding the 27 pts who completed CT, 87% received the planned 6 cycles of CT (median 6 cycles, range 1–6) with an RDI of 81.7% (range 12–106). There was no grade 3/4 hematological toxicity. The only grade 3/4 non-hematological side effects were 3 thromboembolic events. As expected, the most common side effects (grade 1/2) were fatigue (97%), skin toxicity with dryness or desquamation (60%), hand-foot syndrome/palmar-plantar erythrodysesthesia (52%), diarrhea (52%), and nausea (41%). To date, with a median follow-up of 15.3 months, only one relapse has been reported. The only baseline CGA difference between pts who finished the CT vs pts who either a) had to stop CT due to toxicity, b) did not achieve a RDI over 80% or c) had a grade 3 or 4 toxicity, is the VES 13 scale: the mean VES value for pts who received a suboptimal treatment was 3 compared to 2 for pts who received an acceptable treatment.

Conclusion: Based on these preliminary results, adjuvant X is well tolerated in this population. Unexpected was the rate of thromboembolic events. No changes in CGA results as a consequence of treatment were observed. Of all components of the CGA, the VES13 scale may predict the likelihood of satisfactorily completing treatment. Enrollment is ongoing up to a planned total of 43 pts and updated data will be presented at the meeting.