1316 PUBLICATION

## Effect of toremifene (TOR) on the gonadotropins and prolactin in advanced breast cancer patients

I. Számel[1], I. Hindy[1], A. Hajba[2], L. Kangas[3], R. Lammintausta[3]. [1]*National Institute of Oncology, Budapest, Hungary;* [2]*Orion Corporation, Orion Pharma International, Espoo;* [3]*Hormos Medical Ltd, Turku, Finland*

**Purpose:** To differentiate the antiestrogenic and partial estrogenic effect of TOR at the level of the CNS, LHRH tests were carried out during a phase II clinical trial.

**Methods:** In 15 postmenopausal patients LHRH induced FSH, LH and prolactin (PROL) release was monitored prior to TOR treatment (60 mg/day p.o.) and then 4, 8, 12 and 16 weeks afterwards. Hormone levels were analysed by RIA methods.

**Results:** TOR sensitized the pituitary (HP) to the action of the gonadotropins: FSH and LH release showed a tendency to increase during therapy. LH release was significantly increased in the responders. In non-responders the response to a LHRH test was abnormal or lacking. A decreased level of PROL was observed.

**Conclusion:** The drug exerts its effect at the level of the HP, and the antiestrogenic effect of TOR is more dominant than the intrinsic estrogenic property.

1317 PUBLICATION

## Efficacy and toxicity of some chemotherapeutic regimes in heavely pretreated anthracycline-resistant metastatic breast cancer (ARMBC)

V. Moiseyenko, R. Orlova, N. Ermakova, S. Procenko, T. Mikchajlithenko, A. Semjonova. *Department of biotherapy and bone marrow transplantation, N.N. Petrov Research Institute of Oncology, St.-Petersburg, Russian Federation*

**Aims:** To evaluate the effecacy and toxicity of different regimes of chemotherapy for patients (pts) with ARMBC in the non-randomized trial.

**Methods:** The study included 53 pts with morphologically confirmed ARMBC (median age 55 years, ECOG > 2, progressive disease after treatment with Dox in dose >100 mg/m$^2$), who recieved five different regimens of chemotherapy – A: 9/53 pts – 3M (Mit. C 8 mg/m$^2$ + Metotrexate 35 mg/m$^2$ + Mitoxantron 8 mg/m$^2$ 1 d); B: 11/53 pts – Ifosfamide 2 g/m$^2$ 1–3 d + Mitoxantron 12 mg/m$^2$ 1 d; C: 11/53 pts – Vinorelbine 25 mg/m$^2$ 1.8 d + Dox 40 mg/m$^2$ 1 d; D: 10/53 pts – 5-FU 1250 mg/m$^2$ C.I. 1–5 d; E: 14/53 pts – Taxanes (Docetaxel 100 mg/m$^2$ or Paclitaxel 175 mg/m$^2$ 1 d with corticosteroids premedication).

**Results:**

| | A | B | C | D | E |
|---|---|---|---|---|---|
| CR | – | – | – | – | – |
| PR | 11.1% | – | 27.3% | – | 21.5% |
| SD | 66.6% | 33.3% | 18.2% | 50% | 28.5% |
| PD | 22.3% | 66.7% | 51.5% | 50% | 50% |

Median response duration: A – 4 month, C – 5.5 month, E – 7 month.

The greatest hematological toxicities (grade 3 and 4) occurred in 34.6% cycles with neutropenic fever in 15.3% cycles in the B group; A – 14.4% (3.7%), C – 13.8% (3.4%), D – 0%, E – 22.4% (10.2%). Other non-hematology toxicities: mucositis grade 3: A-3.7%, B-7.6%, C-0%, D-0%, E-4.1%.

**Conclusions:** Navelbin + Dox and single agent Taxanes are the most effective chemotheraputic regimes with acceptable tolerability for heavely pretreated ARMBC.

1318 PUBLICATION

## Pharmacokinetic (PK) interaction between epidoxorubicin (EPI) and docetaxel (TXT) in patients with metastatic breast cancer (MBC)

L. Cattel[1], M. Airoldi[2], P. Brusa[1], V. Tagini[1], V. Recalenda[1], S. Marchionatti[2], C. Bumma[2], F. Pedani[2]. [1]*Univ. Hosp. Pharmacol.;* [2]*Oncol. Dep., Turin, Italy*

Thirty-six pts with MBC were treated with EPI 75 mg/m$^2$ iv bolus + TXT 75 mg/m$^2$ (1 hr infusion after 1 hr interval) d.1; q. 3 wk. Results = 6CR (17%), 20PR (55%), 4NC (11%), 6PD (17%). PK parameters:

| Drug | Cp ss (ng/ml plasma) | AUC 0–24 h (ng × h/ml) | Clearance (l/m$^2$/h) | $t_{1/2}$ $\beta$ | $t_{1/2}$ $\gamma$(h) |
|---|---|---|---|---|---|
| TXT | 1212 | 3631 | 57.5 | 38 m | 24 |
| EPI | 2387 | 3278 | 92.9 | 2.4 h | 14.4 |

**Conclusion:** EPI + TXT is very active in MBC; a transient but significant increasing of EPI plasma concentration during TXT-infusion is evident; the Css of TXT were significantly higher in a pt who had G3 gastrointestinal toxicity and in a pt with liver mts (13,100 and 2,400 ng/ml respectively); a significant exponential correlation between WBC number and TXT-Css was observed.

1319 PUBLICATION

## Comparison between CEF or CMF in adjuvant chemotherapy of breast cancer patients with more than three nodes positive

A. Ghavamzadeh, K. Alimoghaddam, P. Nasseri, S. Dosti. *Department of oncology, Tehran university of medical science, Tehran, Iran*

**Purpose:** To evaluate DFS and relapse rates in high risk breast cancer patients (more than three nodes positivity) after chemotherapy with CMF (Cyclophosphamide 600 mg/m$^2$, methotrexate 40 mg/m$^2$ and 5 FU 600 mg/m$^2$ Q 3 weeks for 6 cycles) or CEF (cyclophosphamide 600 mg/m$^2$, Epirubicin 60 mg/m$^2$ and 5 FU 600 mg/m$^2$ Q 3 weeks for 4 cycles and then three aditional CMF cycles).

**Methods:** In this retospective study, after MRM surgery, patients underwent chemotherapy, and then radiotherapy to chest wall (if primary tumor size was more than 5 cm). For ER positive patients tamoxifen are prescribed. DFS compared by Kaplan-Meier method and log-rank test and relapse rates by pearson test.

**Results:** From 508 breast cancer, 78 were high risk (>3 nodes). (mean age = 46.5, premenopause = 64 cases post-menopause = 14 cases). Tumor size, ER positivity and number of involved nodes were equal, between two groups. 51 patients received CMF and 27 patients received CEF. Mean DFS of CMF patients was 35.4 months (CI 95%: 25.7–45.1) and DFS of CEF 32.5 (CI 95%: 24.7–40.4) (p = 0.32). Relapse rates were 72.53% (37 relapses) in CMF and 29.63% (8 relapses) in CEF patients (p = 0.0002).

**Conclusion:** Although DFS was similar between two groups, but it seems that CEF is superior to CMF because lower relapse rate.

1320 PUBLICATION

## Vinorelbine (VNB) plus raltritexed in advanced breast cancer (ABC), a phase II study. Preliminary results

V.D. Ferrari, P. Marpicati, E. Montini, G. Rangoni, E. Simoncini, G. Marini. *Oncologia Medica – Fondazione Beretta, Spedali Civili, Brescia 25123, Italy*

**Introduction:** Raltitrexed (Tomudex) is a direct Inhibitor of thymidylate synthase with activity in in the treatment of colorectal cancer and other tumours. VNB is an active drug in ABC and a synergism was demonstred between FU + VNB, this combination is effective in metastatic breast cancer. The purpose of this study was to evaluate the toxicity, the efficacy and feasability of the combination of VNB + Tomudex in heavely pretreated pts.

**Methods:** since september 1998, 17 pts with ABC were included in an ongoing phase II trial. Median age was 56.5 (range 27–79), median BCOG performance status was 1 (range 0–2), dominant site of disease was visceral in 10, soft tissue in 9, bone in 5, all pts had measurable disease and they had been previously treated with at least one chemotherapic regimen with median number of 2 (range 1–4), median number of prior line of endocrine therapy was 2 (range 0–3). Protocol treatment consisted of VNB 25 mg/m$^2$ IV d 1, 8 and Tomudex 1 mg/m$^2$ IV d 1, 8 every 3 weeks up to 6 cycles, or until to progression. 68 courses have been administered with a median of 5 cycles (range 1–6) for pts.

**Results:** 14 pts are assessable for toxicity and 8 for responce. No toxic death occurred, 1 pt died of progressive disease.. We observed only 1 case of neutropenia grade 4 and 5 cases of reversible elevated transaminases grade 3 NCI that were the most important side effects, 2 pts achieved PR, 2 MR and 2 NC. The chemotherapy schedule is feasible the responces, the moderate toxicity and disease stabilisation are encouraging in heavily pretreated pts.