Patients (pts) characteristics: mean age was 52 (33–68), ECOG PS0: 13, PS1: 12, 17/25 pts received prior CT for their primary disease (with anthracyclines in 16 cases). In all cases, the left ventricular ejection fraction (LVEF) was ⩾50% at the entry.

The dose limiting toxicity evaluated at the first cycle being reached at dose level 5 (with 2 febrile neutropenias without documented infection), dose level 6 tested T 225 mg/m^2 and F 50 mg/m^2. So far, 78 courses have been analyzed: 26 grade 3 (33%) and 14 grade 4 (18%) neutropenias have been observed (only 3 courses with fever). Extrahematological toxicities were 1 grade 3 nausea / vomiting, 1 grade 3 asthenia, 5 grade 2 and 1 grade 3 neurotoxicities. Three pts previously treated by anthracyclines experienced cardiac toxicity: 1 myocardial ischemia, 1 heart failure and 1 asymptomatic decrease of LVEF at 41%.

To date, 22 pts are evaluable for response: 9 partial (41%) (PR), 11 (50%) stabilisations.

For the dose levels 3, 4 and 5, PR rate is 60%.

In conclusion, TAXOL® dose escalation is still being investigated with FARMORUBICIN® kept at 50 mg/m^2.

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LHRH AGONIST ANALOGUE FUNCTIONAL TEST IN ADVANCED BREAST CANCER PATIENTS TREATED WITH TOREMIFENE (TOR)

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In order to differentiate the antagonistic and agonistic effect of TOR at the level of the hypothalamus-hypophysis (HT-HP) axis, LHRH test was performed during a phase II clinical trial. In 15 postmenopausal patients with advanced breast cancer FSH and LH release—induced by LHRH agonist (Suprefact-R 0.5 mg sc.)—was monitored during a 16-week TOR treatment (60 mg/day po). The functional test was carried out prior TOR therapy and then 4, 8, 12, 16 weeks afterwards. FSH and LH were measured by RIA method.

On the basis of our endocrine study, TOR has a strong antagonistic (antiestrogenic) mechanism of action at the level of the HP, and a tissue-specific agonistic effect in the periphery. The drug sensitizes the HP for the LHRH stimulus without eliciting any clinical or hormonal side effect.

The LHRH test supported our earlier findings, obtained by the TRH provocation test, i.e. TOR exerts its effect predominantly at the level of the pituitary gland.

372 POSTER

NEO-ADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BEAST CANCER (LABC): FEC (5FU, EPIRUBICIN, CYCLOPHOSPHAMIDE) VS HIGH DOSE INTENSITY EC + G-CSF (FILGRASTIM). AN EORTC—NCIC—SAKK STUDY. PRELIMINARY RESULTS OF DOSE INTENSITY (DI)

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Patients: Since May 1993, 205 patients (pts) with LABC (clinical inflammatory, T_4 N_x M_0 or any N_2/N_3 M_0) have been randomized into the study. *Treatment:* F (500 mg/m^2 i.v. d 1, 8), E (60 mg/m^2 i.v. d1, 8) and C (75 mg/m^2 p.o. d 1–14) q 28 d × 6 (arm A) *vs* E (120 mg/m^2 i.v. dl), C (830 mg/m^2 i.v. d 1) and G-CSF (5 μg/kg/d s.c. d 2–13) q 14 d × 6 (arm B). *Results:* In arm A (43 pts off-treatment), the delivered DI (mg / m^2 / week, median value) for F, E and C were respectively 212 (range: 152–264), 26 (18–31) and 220 (156–293). The corresponding figures in arm B (56 pts) for E and C were 57 (29–62) and 384 (206–426). The percentage of delivered DI relative to the theoretical DI was around 85% for all drugs in arm A and 94% for both drugs in arm B. Relative to arm A, the DI for E and C in arm B were increased by 119% and 75% respectively. Hematological grade 3–4 toxicities were (% pts, arm A/ B): neutropenia (86%/ 61%), thrombocytopenia (26%/ 36%) and anemia (26%/ 55%). 1 pt in arm A and 11 pts in arm B experienced a significant but asymptomatic decrease in left ventricular ejection fraction. *Conclusion:* Dose intensification of E and C with G-CSF support in LABC pts is feasible, with acceptable toxicity.

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PHASE II TRIAL OF LETROZOLE (A NOVEL ORAL NONSTEROIDAL AROMATASE INHIBITOR) IN POSTMENOPAUSAL PATIENTS WITH ADVANCED OR RECURRENT BREAST CANCER

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64 Japanese postmenopausal patients (pts) (median age 59: range 38–76) with advanced or recurrent breast cancer who had received more than 1 prior regimen (hormonotherapy and/or chemotherapy) were randomized between 2 oral regimen of letrozole for more than 8 weeks, 33 pts (ER+: 18, ER−: 3, unknown: 12) being given 0.5 mg of letrozole daily and 31 pts (ER+: 15, ER−: 3, unknown: 13), 1 mg daily. The tumor responses were peer reviewed and response rates (CR + PR) in evaluable cases were 28% (3CR + 6PR/32, 95% C.I.: 14–47%) in 0.5 mg group and 39% (5CR + 6PR/28, 95% C.I.: 22–59%) in the 1 mg group, respectively. Stabilization of the disease for more than 6 months (long NC) was obtained in 19% for the 0.5 mg group and in 29% for the 1 mg group, respectively. Progressive disease was noted in 31% for the 0.5 mg group and in 21% for the 1 mg group, respectively. Clinical adverse experiences were observed in 6% of pts (2/33, 5 events) for the 0.5 mg group and in 6% of pts (2/31, 2 events) for the 1 mg group, all being only of mild severity (grade 1) except one event of grade 2 itching in the 1 mg group. Laboratory test abnonnalities were found in 9% of pts (3/33, 6 events) for the 0.5 mg group and in 10% of pts (3/31, 6 events) for the 1 mg group, respectively. Except for one event of grade 2 GOT and GPT elevation noted in the 0.5 mg group, all other events were of either grade 0 or grade 1 severity. Estrone levels were maintained below the detection limit (2.5 pg / ml) and a sustained estradiol suppression was observed, with levels near the detection limit (1 pg / ml) during treatment. There was no clinically relevant changes in the other hormones (aldosterone, cortisol, FSH, LH, testostetone, androstenedione). These highly promising results support further extensive clinical evaluation.

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VINORELBINE, 5 FLUOROURACIL, LEUCOVORIN AND CYCLOPHOSPHAMIDE AS FIRST LINE CHEMOTHERAPY IN METASTATIC BREAST CANCER (MBC)

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Vinorelbine (Navelbine) alone or in combination with Adriamycin or 5 FU has major activity in MBC. From 06.92 to 04.94, 60 patients were included. Eligibility criteria: MBC, no prior chemotherapy for metastatic disease, measurable target lesion, WHO PS ⩽ 2, informed consent, 55 patients are eligible. Patients characteristics: median age: 52.3 years (33–74) PS 0: 35 (63.6%) 1: 16 (29.1%) 2: (7.3%). Prior treatment: surgery 40 (72.7%), post operative radiotherapy 32 (58.2%), adjuvant chemotherapy 27 (49.1%), hormonotherapy 23 (41.8%). Metastatic at diagnosis: M0: 39 (70.9%) M1: 15 (27.3%) unknown: 1 (1.8%). Hormonal status at inclusion: premenopausal 14 (25.5%), post menopausal 41 (74.5%). Median metastatic sites 3 (1–6). Visceral metastases: 65%. Treatment schedule: Cyclophosphamide 500 mg/m^2 D1—Vinorelbine IV 25 mg/m^2 D1, 8—5 FU 500 mg/m^2 D1, 8—leucovorin 200 mg/m^2 D1, 8—repeated every 21 days. Total number of courses: 276—mean number of courses: 5.7. Treatment was very well tolerated with no grade superior to 2 except for alopecia. Efficacy: Number of patients: 60: OR rate: 45% (95% CI 32.4–57.6). CR: 6.7% (0–13). PR: 38.3% (22.5–54.1). Median time to first response: 26.7 w (r: 13–36). Median duration of: CR: n = 4–45.4 w (r 20.3–45.4+) – PR: n = 23–37.4 w (r 15.1 – 75.1+) OR: n = 27 44.1 w (r 15.1–75.1+). Median survival: 66.4 w (r 3+ – 80+). Alive: 34 patients (56.7%). Median remission duration: 187 days (91–222). *In conclusion:* efficacy in terms of both O.R. rate and duration of O.R. is within the range of expected results with multidrug regimens without anthracyclins.