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PREOPERATIVE CHEMOTHERAPY OF OPERABLE BREAST CANCER (STAGE IIIA). PROGNOSTIC FACTORS OF DISTANT RECURRENCE.
M. Tubiana-Hulin, M. Malek, M. Briffod, F. Spyratos, K. Hacene, C. Pallud, S. Lasry, J. Rouëssé - Centre René-Huguenin - 35, rue Dailly - 92210 Saint-Cloud

150 consecutive breast cancer patients stage IIIA were treated with a combined modality protocol : including neoadjuvant chemotherapy (AVCMF), surgery, post operative chemotherapy (AVCMF), radiotherapy and hormonotherapy for post menopausal patients.
Median tumor size was 64,7 mm (135 patients had T_3 tumors). 47 % of patients had an objective clinical tumor regression allowing conservative surgery in 35 % of cases.
Flowcytometric high S phase and cytomorphologic changes on sepuential cytopunctures were significantly related to tumor regression (p=0,01 respectively).
At the median follow-up (50 months), OS rate was 81,5 %, DFS rate 67,9 % and MFS rate 71 %.
A univariate analysis showed that distant metastases were significantly relate to pretreatment variables : N1, high S phase, and large nuclear area, and to post chemotherapy variables : N+ and fat axillary metastases, and vascular emboli in the breast tumor. A cox regression analysis was performed on a group of 71 patients, not differing from the entire group, with all the data. The first two unfavorable selected variables for MFS were high S phase (p=0,0001) and nodal involvement of the top of axilla (p=0,003). The third selected variable, clinical tumor regression, influenced positively distant outcome p=0,01.
In this series, response to initial chemotherapy was more frequent in the highly proliferative tumor group, which prognosis remained globally unfavorable. However, in this heterogeneous group, some patients appeared to have a MFS benefit.

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THE VALUE OF CATHEPSIN D AND pS2 EXPRESSION ON SMEARS OF PRIMARY BREAST CANCER: CORRELATION WITH VARIOUS PROGNOSTIC FACTORS.
P.Athanassiadou, E.Petrakakou, D.Lazaris, N.Louvrou, P. Athanassiades, K.Keramopoulos, K.Kyrkou.
Departments of Cytology and Cytogenetic and 1st Obstetrics and Gynaecology, Athens University, Athens, Greece.
The aim of this study was to detect the expression of protease Cathespin D and pS2 protein in a series of 100 breast cancer imprint smears using an immunocytochemical technique. In all cases staining expression was correlated with the oestrogen (ER) and progesterone (PR) receptor status of the tumour, the degree of lymphonode infiltration and the histological type of the tumours. The presence of ER+ve and PR+ve receptors was associated with positive Cathespin D (71.4%) and pS2 (46.4%) immunostaining. Positive expression of Cathepsin D (55.5%) and pS2(38,9%)was found in smears with ER+ve and Pre-ve tumours.Negative reaction of Cathepsin D and pS2 was found in 85% and 80% respectively of imprint smears with ER-ve and Pr-ve tumours. The relationship of both markers immunostaining with the degree of lymph node infiltration and the histological type of the tumour is discussed. In conclusion we have shown that expression of Cathepsin D and pS2 in breast cancer could be more effective markers of hormone dependence breast tumours.
Key words: breast cancer, tumor markers, immunocytochemistry

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ADJUVANT CHEMOTHERAPY WITH AUTOLOGOUS BONE MARROW REINFUSION IN PATIENTS WITH PROGNOSTICALLY UNFAVOURABLE BREAST CANCER.
E.G.E. de Vries, D.Th.Sleijfer, P.H.B.Willemse, P.O.M.Mulder, W.T.A.v.d.Graaf, C. Smit Sibinga, E.v.d.Ploeg, W.V.Dolsma and N.H.Mulder. University Hospital, Groningen, The Netherlands

Twenty-four patients with breast cancer with more than 5 involved nodes including the most apical (level III) axillary lymph node received, after surgery, 6 courses of induction chemotherapy (IC) followed by ablative chemotherapy (AC) and reinfusion of autologous marrow (ABMT). IC consisted of MTX 1.5 g/m² and 5-FU 1.5 g/m² on day 1, prednisone 40 mg/m² orally day 2-14, doxorubicin 50 mg/m² and vincristine 1 mg/m² on day 14. Courses were repeated 6 times q.4 weeks. Ten patients received as AC cyclophosphamide 7 g/m² and VP16-213 1.5 g/m². In 14 patients AC consisted of mitoxantrone 50 mg/m² and thiotepa 800 mg/m². ABMT followed on day 7. Finally, patients received radiotherapy and two years of tamoxifen. Median age of patients was 42 yrs, range 29-52 yrs. The median number of involved nodes was 10. One patient died during AC, 6 developed septicemia, 2 had mucositis gr 3, the others gr 1 or 2. In the follow-up, 1 patient died from cardiac failure, radiation induced pneumonitis occurred in 50%. Two patients have relapsed systemically after 18 and 42 months, both in Cy/VP regimen. Median observation is 36 months, disease free survival at 5 years is predicted to be 84%. Intensive treatment in these patients with high numbers of involved axillary lymph nodes may substantially improve their chance of disease free survival.

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EXPERIMENTAL PHARMACOLOGY OF VOROZOLE, A NON-STEROIDAL AROMATASE INHIBITOR
De Coster R., Wouters W., Van Ginckel R., Bowden C.* and Tuman R.*
Janssen Research Foundation, Beerse, Belgium and *Spring House, USA
Vorozole, the (+)-(S)-enantiomer of a triazole derivative, is a potent and selective aromatase inhibitor with Ki values of about 1nM in rat ovarian homogenates, human placenta microsomes, rat and human granulosa cells and cells from human adipose tissue. In pregnant-mare's serum gonadotropin primed female rats, vorozole lowers serum estradiol levels by more than 90 % 2 hours after oral administration of 0.05 mg/kg. In male cynomolgus monkeys i.v. racemic vorozole (0.003 mg/kg) inhibits peripheral aromatisation by 85%. In the DMBA-induced rat mammary carcinoma model, vorozole (2.5 mg/kg b.i.d.) reduces tumor growth by 90%, lowers the number of existing tumors and prevents the appearance of new tumors similarly to ovariectomy. The high selectivity of vorozole was demonstrated both *in vitro* and *in vivo*. Vorozole is a highly selective aromatase inhibitor both *in vitro* and *in vivo* with either basal or stimulated testicular and adrenal biosyntheses, including aldosterone, only slightly modified at 10^{-5}M *in vitro* and 10 mg/kg *in vivo*.

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POPULATIONAL IMPACT OF ADJUVANT CHEMOTHERAPY FOR EARLY BREAST CANCER: AN OVERVIEW FROM A EUROPEAN COMMUNITY SPONSORED MASS SCREENING PROGRAMME.
J. Illarramendi, M. Tejedor, M. Dominguez, F. Arias, E. Martinez, R. Lopez, B. Larrinaga, N. Ascunce, A. Del Moral, J. Valerdi.
Service of Oncology. Hospital de Navarre. Pamplona. Spain.
Collected experience from clinical trials has shown that adjuvant chemotherapy (AdjCh) for early breast cancer (BC) is able to save many lives in Europe (E). **Material & methods:** Target population: 244 BC patients diagnosed during the first round of a pilot programme of BC screening in the region of Navarre were considered for AdjCh, according to the latest published consensus. Therapy: Homogeneous for all the population, with one reference centre and one regional tumour registry. CMF, CAF, AC or a shortened intensive scheme, in relation to nodal status, age, size and hormone receptors. **Results:** Overall compliance: 234/244 (95.9%). Delivered dose-intensities: CMF 94.5%, CAF 88.9%, AC 98.4%, intensive scheme 75.3%. Toxicities requiring admission: 9/234. No therapy-related mortality. Early relapse free survival (median follow up 17 m): N0 97.8%, N1 93.8%. Estimated pharmaceutical cost: 66,100 ECU. Theoretical effect of Adj Ch on crude Sv for the overall population with BC: 3.5-9% **Conclusions:** Delivery of AdjCh was optimal in one of the five european populations taking part in the E against Cancer pilot programme of BC screening. This factor will add an effect in the reduction of mortality rates, and has to be taken into account when developing populational policies against BC in E.