with high values of uPA and/or PAI-1 are randomized to 6 cycles CMF versus observation. Patients with low content of both uPA and PAI-1 are distributed to observation only. In this trial, 13 German clinical centers take part; to date 628 patients are recruited. It is now going to be extended to an European trial, supported by the BIOMED-2 program.

| P46 | 15 year update of the naples GUN trial of adjuvant breast cancer therapy: Evidence of interaction between c-erb-B2 expression and Tamoxifen efficacy |

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From February 1978 to December 1983, 433 patients (pts) were enrolled in the GUN trial. Ten year results have already been reported (Bianco et al., Lancet, 1988). Postmenopausal pts (n = 308) with (N+) or without (N−) lymph node metastases were randomized to receive either Tamoxifen (TAM), 30 mg qd for 2 years or no therapy. Premenopausal N+ pts (n = 125) were randomized to receive either CMF × 9 cycles or CMF × 9 cycles plus Tamoxifen (TAM), 30 mg qd for 2 years. Overall 206 pts were randomized to receive TAM versus 227 pts not receiving the antioestrogen (no TAM). c-ErbB2 expression was evaluated on 245 paraffin-embedded specimen by immunohistochemistry. At 15 years, when the median follow-up was about 11 years, TAM was effective in improving both Disease Free Survival (DFS) (p = 0.0008) and Overall Survival (OS) (p = 0.05). When pts were stratified according to menopausal and lymph-node status DFS and OS benefits were observed in all subgroup of pts receiving TAM. More interestingly, when we evaluated the c-erbB2*TAM interaction the following results were found:

	Relapses Obs/Exp		Deaths Obs/Exp	
	c-erbB2− (n = 182)	c-erbB2+ (n = 63)	c-erbB2− (n = 182)	c-erbB2+ (n = 63)
TAM	0.83	1.17	0.85	1.56
no TAM	1.18	0.89	1.15	0.64

According to these data TAM seemed to improve DFS and OS only in c-erbB2− pts, while showing a paradoxical detrimental effect in c-erbB2+ pts. A multivariate test for interaction adjusting by lymph node status, menopausal status, nuclear grade, estrogen receptor (ER) status and ER*TAM interaction confirmed the predictive value of c-erbB2 expression (OS p = 0.007; DFS p = 0.04). In conclusion, a) at 15 years adjuvant TAM reduces relapse and death rates independently by nodal and menopausal status; b) in our randomized trial c-erbB2 expression is a strong predictor of adjuvant tamoxifen failure independently by ER, ER*TAM interaction and other major prognostic variables.

| P47 | Locally advanced breast cancer (LABC): Prognostic variables affecting results |

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Purpose: To evaluate the prognostic significance of clinical and hystopathological indicators on disease free survival (DSF), overall survival (OS) and objective response (OR) rates in Locally Advanced Breast Cancer (LABC) patients (pts) treated with a multimodality therapy.

Patients and Methods: Three-hundred sixty-seven assessable LABC pts entered onto two consecutive randomized trials performed in our Medical Oncology Dept. and North-West Oncology Group (GONO) cooperative centers. In the first study 117 pts were randomly allocated to receive either 3 courses of primary FAC (5-FU 600 mg/sqm, ADM 50 mg/sqm, 5-FU 600 mg/sqm day 1 every 21) followed by local-regional treatment (surgery and/or radiotherapy) and 6 courses of adjuvant chemotherapy consisting of 3 FAC alternated with 3 CMF (CTX 600 mg/sqm, MTX 40 mg/sqm, 5-FU 600 mg/sqm day 1 every 21) or the same program in which chemotherapy was preceded by oral Dethylstilbestrol (DES 1 mg/day for 3 consecutive days). In the second study 150 pts were randomized to receive either a standard primary FEC (5-FU 600 mg/sqm, EpiDX 60 mg/sqm, CTX 600 mg/sqm day 1 every 21 days) or an accelerated FEC every 2 weeks with GM-CSF (5 um/kg/day for 10 days s.c.).

Results: ORs to primary chemotherapy was 64% (95% C.I. 58–70%). On univariate analysis, performed on pts characteristics at diagnosis, pts with inflammatory breast cancer (IBC) had a significantly lower probability of response than pts who did not (p = 0.04); no other differences in response rates were observed between pre-menopausal and post menopausal pts, estrogen (ER) an/or progesterone (PgR) receptor positivity, stages of disease (IIIA vs IIIB). The median PFS and OS of the whole group were 3.5 and 5.1 years respectively. On univariate analysis, performed at surgery, no correlations were observed between age, menopausal status, stage of disease (IIIA vs IIIB), response to primary chemotherapy (pathological complete response, residual disease >/≤1

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cm) and DFS or OS. Pts with. ER and/or PgR receptor positivity had a better OS rates compared to pts with ER and/or PgR negative tumors (p = 0.02 and p = 0.03 respectively): hormonal receptor positivity did not affect DFS. Pathological evidence of IBC significantly correlates with OS (p = 0.0005) but not with DFS (0.07). The number of positive nodes at surgery significantly predicts both DFS and OS (p = 0.0003 and p = 0.003 respectively).

Conclusion: in LABC pts treated with a multimodality therapy hormonal receptor positivity at surgery significantly correlates with a better OS;IBC significantly correlates with a poor outcome however is nodal status at surgery the strongest prognostic factor associated with PFS and OS. A multivariate analysis will be presented.

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| P48 | Prognostic value of estrogen receptor (ER) status in breast cancer patients with five or more axillary lymph nodes (LN) involved |

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Objective: To find parameters influencing the risk of relapse in breast cancer patients with five or more positive axillary LN treated with adjuvant intensive chemotherapy.

Methods: 31 patients up to 65 years of age received six cycles of an antracycline containing chemotherapy regimen followed by intensive chemotherapy with peripheral blood progenitor cell rescue and local irradiation. Patients with ER+ tumors continued on adjuvant therapy with tamoxifen later. Survival analysis identified ER status as prognostic factor for relapse in our series. ER+ and ER− patients were homogeneous for age, menopausal status, number of involved axillary LN, and expression of Ki-67, c-erb-b2, and p53.

Results: Median number of positive axillary LN was 10. Median relapse free survival was 23 months for ER− patients and no ER+ patient has relapsed with a median follow up of 23.5 months (p = 0.0008). ER+ patients tended to have lower stages of the disease but the adjusted analysis yielded ER status as an independent factor for risk of relapse.

Conclusion: Our preliminary data show that in our series ER status appears to be the main predictor of relapse. We can not rule out that adjuvant treatment with tamoxifen is responsible for the better outcome of ER+ patients.

| P49 | Predictive parameters of response in primary CMF chemotherapy of breast cancer |

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Introduction: In breast cancer, primary chemotherapy has proved to be useful in the evaluation of drugs effectiveness. It also permits a greater rate of conservative surgical procedures.

Objective: To assess factors that may predict the response to primary chemotherapy.

Design: Longitudinal study.

Patients and Methods: From January 1990, 150 patients with breast cancer were treated with primary chemotherapy. Conditions to join the study were tumor size greater than 3 cm. and age less than 66. Tumor diameter was measured by mammography. All patients had a positive cytology or a minute open biopsy that was also used for the evaluation of nuclear grade and the immunocytochemical determination of hormone receptors and c-erb-B2 expression. Patients were treated with CTX, 600 mgr/m2; MTX, 40 mgr/m2; and 5-FU, 600 mgr/m2; on days 1 and 8, for three cycles.

The tumor response was evaluated by mammography.

Results: A good response was assessed in 52% of cases (6% CR, 46% PR ≥50%). The proportion of responses was 30% in grade 1 tumors; 49% in grade 2 tumors and 73% in grade 3 tumors (p < 0.01). Negative/positive estrogen receptors were associated with responses of 66% vs. 41% (p < 0.002).

Tumor diameter, progesterone receptors and c-erb-B2 expression were not related to response.

Conclusion: High nuclear grade and lack of estrogen receptors expression are predictive parameters of good response to primary CMF chemotherapy in operable breast cancer.

| P50 | Effectiveness of postoperative radiotherapy in controling subclinical locoregional disease in breast cancer patients with positive axillary nodes |

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Background: Results of randomized trials indicate that postmastectomy radio-