well balanced: age < 72; PS 0–3; evaluable lesions; no prior anthracycline therapy; absence of cardiopathy. Patients were given cyclophosphamide and 5-fluorouracil 500 mg/m^2 each and either doxorubicin or pirarubicin 50 mg every three weeks-6 cycles.

Efficacy: FAC group: CR −6/44, PR −15/44;

FPC group: CR −7/43, PR −12/43; statistically N.S.

Toxicity (myelosupression, nausea-vomiting, cardiotoxicity) was similar in both groups. Alopecia: FAC group: gradus 2 −8/43, gradus 3 −29/43;

FPC group: gradus 2 −10/44, gradus 3 −11/44;

$P < 0.0000001$ significantly favouring FPC.

Pirarubicin gives better life quality to patients with advanced breast cancer and should be an anthracycline of choice in young, high risk patients with early breast cancer submitted to the adjuvant chemotherapy, causing less alopecia.

384 PUBLICATION

PILOT STUDY OF TAXOTERE IN TAXOL-RESISTANCE METASTATIC BREAST CANCER (TRMBC)

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Ten patients (pts) with MBC who had primary/secondary resistance to Taxol (135–250 mg/m^2 over 3–24 hours) were treated with Taxotere 100 mg/m^2 every 21 days. *Pts characteristics (10):* med age, 47 yrs (37–61); med Zubrod PS, 1 (0–2); med # sites 3 (2–5); disease sites: liver 9/10, bone 4/10, soft tissue/LN 7/10; med # of prior CT was 2 (1–3); 9/10 had prior anthracycline therapy. *Results:* 10 pts were evaluable for response. Responses: 1 MR, 4 NC and 4 PD. *Toxicity:* to date, 10 pts received 30 cycles. *Hematological:* med nadir granulocytes ($\times 10^3$)/dl: 0.3, med nadir platelet count ($\times 10^3$)/dl: 236,000. 4 pts had 8 cycles complicated with neutropenic fever. *Other toxicity (grade 2 or greater) by # pts (# cycles):* stomatitis 3 (5), diarrhea 4 (5), fatigue 8 (14), myalgias 7 (12), skin 5 (9), paresthesias 7 (13). *Conclusion:* The preliminary data of this ongoing trial showed that Taxotere has activity in TRMBC.

385 PUBLICATION

PILOT STUDY OF CONTINUOUS INFUSION 5FU AND BOLUS DOXOCUBICIN AND CYCLOPHOSPHAMIDE FOR BREAST CANCER

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The therapeutic index of 5FU is improved with continuous iv infusion (ci) compared with bolus administration. We have combined 18 weeks ci5FU with 6 courses of bolus doxorubicin (50 mg/m^2) and cyclophosphamide (600 mg/m^2) q3/52, aiming to develop a regimen for neoadjuvant treatment of breast cancer. 25 patients have been treated 6 large operable tumours, 5 locally advanced disease, and 13 metastatic disease.

5FU mg/m^2/day	Patients treated	Neutropaenia grade 3	Neutropaenia grade 4	Mucositis grade 2	Mucositis grade 3
100	6	4	1	4	0
150	4	1	2	3	0
200	14	5	7	7	2

The 3rd dose level produced tolerable toxicity. WHO grade 3–4 neutropaenia was frequent but short-lived in the majority. Mucositis required 5FU dose reduction in 2 patients. Two patients had neutropaenic sepsis and one died of unresolving pneumonia. Grade 2 plantar palmar skin toxicity occurred in 5 patients and grade 2 diarrhea in 2. Hickman line-associated proximal vein thrombosis occurred in 4 patients despite prophylactic warfarin (1–3 mg/d). The response rate in 20 evaluable patients was 5 CR, 9 PR, 3 SD, 2 PD. Patient accrual will continue to further define the response rate in neoadjuvant patients.

Head and neck tumours

386 ORAL

PREVENTION OF SECOND PRIMARY TUMORS WITH A SECOND GENERATION RETINOID IN SQUAMOUS CELL CARCINOMA OF ORAL CAVITY AND OROPHARYNX: LONG TERM FOLLOW-UP

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Retinoids exert a prophylactic action on the development of epithelial cancers when tested on human premalignant lesions, and are now used in the chemoprevention of epithelial cancers, in randomized trials. We prospectively studied 316 patients who developed squamous cell carcinoma of the head and neck, classified as T1/T2, N0/N1 ⩽ 3 cm, M0. Patients were randomly assigned to receive orally, either etretinate (a loading dose of 50 mg per day the first month, followed by a dose of 25 mg per day the following months) or a placebo for 24 months. Adjuvant treatment began no later than 15 days after surgery and/or the initiation of radiotherapy. The five-year survival rate and disease free survival rate are similar in the two groups. There are no differences regarding either local, regional and distant relapses (logrank NS). After a median follow-up of 65 months. forty two patients in the etretinate group and forty in the placebo group, developed a second cancer, with respectively 18 and 17 in the head and neck region. Adjuvant treatment was definitively discontinued mainly due to toxicity in 33% of patients in the etretinate group versus 23% in the placebo group ($P < 0.05$). Etretinate, a second-generation retinoids, does not prevent second primary tumors in patients who have been treated for squamous cell carcinoma of oral cavity and oropharynx.

387 ORAL

CHROMOSOMAL ABNORMALITIES INVOLVING 11Q13 ARE ASSOCIATED WITH POOR PROGNOSIS IN SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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The karyotype is an independent prognostic factor in certain hematologic malignancies and solid tumors, but no such data have so far been reported in squamous cell carcinoma of the head and neck (SCCHN).

Material & methods: The present study included 116 patients. Samples were obtained from diagnostic biopsies or at operation 1987–1991. The samples were short-term cultured in 5–10 days before karyotyping. Due to karyotypic findings patients were divided into four groups: Normal karyotype (k1), numerical changes only (k2), simple structural rearrangements (k3) and complex karyotype (k4).

Results: Survival was significantly shorter in k4 than in k1–3 in the total material ($P = 0.02$), as well as among laryngeal carcinomas, the largest subgroup ($P = 0.045$). The most common breakpoint was 11q13 seen in 11 tumors, 10 of which also showed complex karyotypes. Survival was significantly shorter for patients with 11q13 rearrangements ($P = 0.001$).

Conclusions: Complex karyotype and 11q13 aberrations are independent prognostic factors in cases of SCCHN. The oncogene *prad1*, encoding for Cyclin D1, is located in 11q13, and studies regarding amplification of *prad1* and overexpression of Cyclin D1 are now initiated in our laboratory.