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RANDOMIZED PHASE III STUDY COMPARING 5 FLUOROURACIL (F) CYCLOPHOSPHAMIDE (C) AND EITHER THEPRUBICIN (T) OR DOXORUBICIN (A) IN THE TREATMENT OF ADVANCED BREAST CANCER (ABC), FINAL RESULTS : HOW PATIENT SELECTION AND METHODS OF TUMOR ASSESSMENT COULD INFLUENCE RESPONSE RATE (RR).

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Between 10/89 and 12/91 168 patients (Pts) with ABC were randomized to receive either FTC or FAC (F and C 500 mg/m2, T or A 50 mg/m2 Q3-4w).
All Pts had to be in first line palliative chemotherapy (CT) with measurable or evaluable disease. Pts with isolated non measurable bone disease were also eligible (13 %). Pts characteristics were well balanced between the 2 groups. Safety FTC caused significantly less alopecia than FAC (p <0.0001). All other side effects were identical in both 2 groups. Efficacy : No difference in RR, time to disease progression and overall survival was observed whichever Pts subsets. Conclusion : FTC seems as active as standard FAC and gives much less alopecia. The RR widely varies depending on Pts selection and the rigor of tumor response assessment.

	RR %	
	FTC	FAC
Panel of experts	30.5	30.7
Investigators	37.6	46.1
no adjuvant (adj) CT	39.1	41.4
adj CT without anthracycline	36.3	18.1
adj CT with anthracycline	14.2	19.2
Bone metastases	8.1	16.2
liver metastases	37.2	43.4
lymph nodes	64.2	84.2

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A PHASE II STUDY OF LOSOXANTRONE (DuP 941) IN ADVANCED BREAST CANCER

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Losoxantrone (DuP 941) is one of a series of anthrapyrazoles intercalating agents selected for clinical development based on its broad spectrum of preclinical activity, limited toxicity in Phase I studies, high response rate in a prior Phase II breast cancer (b.c.) study and potentially reduced cardiotoxicity (Talbot 1991). 198 patients (pts) with bidimensionally measurable advanced b.c., normal cardiac function (LVEF $\geq$ 45%) with up to one prior chemotherapy (CT) (excluding anthracyclines) have been treated with a starting dose of 50 mg/m^2 iv q3 weeks. Dose adjustments could be made anytime after the first dose, depending on tolerance.
Data from 138 pts, 70 patients with no prior CT, median age 61, PS 0-2 and 58 pts with prior CT, median age 53, PS 0-2 are available for analysis. The main toxicity is granulocytopenia grade 3 and 4 in 88 pts. Two pts were discontinued because of Congestive Heart Failure, after 8 and 10 courses, cummulative doses 512 and 580 mg/m2. Dose modifications were given according to the nadir of WBC, the median number of doses per patient being 4. Out of 70 pts in the no prior CT group, 1 had a CR and 29 had PR. In the prior CT group, there were 1 CR and 17 PRs. Analysis of trial results is ongoing. In conclusion, Losoxantrone is an active drug for the treatment of b.c. with the main toxicity being granulocytopenia and some degree of cardiotoxicity.

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TAMOXIFEN CONTINUATION DURING SECOND-LINE HORMONE TREATMENT OF ADVANCED BREAST CANCER: A RANDOMIZED STUDY

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Eighty patients (pts) with advanced breast cancer, eligible for second-line hormone treatment with aminogluthetimide (AG) after first-line tamoxifen (T), were randomized to continue T during AG treatment (arm A) or to discontinue it (arm B). Partial responses in evaluable pts were 6/36 (16.7%) in arm A and 4/36 (11.1%) in arm B (p=not significant). Progression free and overall survival were not significantly different. Toxicity was mild and mainly related to AG. Possible benefit from continuation of T during second-line AG in breast cancer could derive from the inhibition of regrowth of T-sensitive, AG-insensitive cells: our results, however, do not support this hypothesis.

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TIME TO RESPONSE TO CHEMOTHERAPY: AN ANALYSIS OF 316 ADVANCED BREAST CANCER PATIENTS

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With the aim to evaluate the time needed to reach tumor response, 316 patients (pts) with advanced breast cancer scheduled to receive combination chemotherapy were analyzed. Pts received a maximum of 11 cycles of the FEC regimen (5-Fluorouracil, Epirubicin and Cyclophosphamide, every 21 days). Overall, 53.8% of pts had an objective response (OR): 25% in the first 3 months, and 50% in 7,5 months. Time to tumor response was longer in pts with the following pretreatment characteristics: prior exposure to adjuvant chemotherapy, nodal positivity at diagnosis, no previous endocrine treatment and bone metastases. These data could help in deciding how long chemotherapy should be continued for palliative treatment of advanced breast cancer.

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VINORELBINE (VNB) AND MITOXANTRONE (MTZ) FOR ADVANCED BREAST CANCER (ABC) THAT HAS PROGRESSED ON AN ANTHRACYCLINE REGIMEN. PRELIMINARY REPORT

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VNB has been previously reported as a new active agent in ABC (Fumoleau ASCO '90. C 76) and MTZ has a 25% response rate in previously treated patients (pts). Between 11/91 and 12/92 NVB + MTZ for pts with ABC was evaluated for response (R) and toxicity (T). VNB 25 mg/m2 day 1-8 and MTZ 8 mg/m2 day 1 EV. Both drugs were repeated on day 21 or 28. All pts had progressed to al least one chemotherapy regimen containing doxorubicin or epirubicin and hormonotherapy. 16/17 pts are fully evaluable. **Results:** Overall response rate 5/16 (CR: 0 PR: 5). R: by dominant metastatic site were: local tumor 3, lymph node 3, lung: 3. Median time to progresion was 112 days (r 68-180). T grade III-IV according WHO criterias were: neutropenia 2, phlebitis 4. Dose intensity of VNB was 50% in 13/16 pts. There were no drug related deaths. **Conclusions:** NVB + MTZ on day 1 each 21-28 days in an active 2nd or 3rd line combinations in ABC previously treated with anthracyclines and it should be further evaluated. Study is still ongoing.

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NAVELBINE (N) + MITOMYCIN (M) IN ANTHRACYCLINES RESISTANT OR REFRACTARY ADVANCED BREAST CANCER (ABC). PRELIMINARY REPORT.

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Between 8/91 and 12/92 a new regimen of chemotherapy for pts. with ABC was evaluated for R and T. N 25 mg/m2 day 1-8-15 and M 7 mg/m2 day 1 EV. Both drugs were repeated on day 28.
All pts had previously received chemotherapy with anthracyclines, 18 pts also had previous endocrine treatment for metastatic disease, 68/72 are evaluable, 22 premenopausal, 46 postmenopausal. Median age 57 (r 32-70). **Results:** Overall response rate was 47% (CR: 7/68 PR:25/68). Median time to progresion was 6 m (r2-14). Overall survival was 6 m (r2-18). Response rate according with metastatic dominant site were: soft tissue 25/35, lung 7/12, liver 4/14, bone 0/7. T: Grade III/IV according WHO scale were: neutropenia 6%, Diarrea 1.5%, neurotoxicity 7.5%. There were no drug related deaths after 277 cycles of treatment (media 4). **Conclusions:** 1) N + M is an active regimen in ABC resistant or refractory to anthracyclines; 2) Main T was neutropenia (50%) and neurotoxicity (10%). More than 50% of pts. had a 33% reduction of dose intensity of N; 3) N should be evaluated as 1st. line combination in pts unable to receive anthracyclines.