%	H	S	W	VB	VR	D	N	E	I
T	57	56	41	8	29	16	8	25	10
A	39	38	23	1	22	14	22	36	22
M	37	43	56	19	12	50	1	44	18

A versus T showed significantly lower incidence of H, S, W, VB and VR [range of $p < 0.005$] and higher incidence of N and I for A[$p < 0.01$]. D was significantly higher for patients on M as compared to both T and A[$p = 0.002$]. Side effects are frequent and may be clinically distressing on any of the three drugs. Against the new aromatase inhibitors the problem of megace tolerance is well recognised but the tamoxifen comparative toxicity is of interest in view of the current adjuvant trials.

1259 ORAL

A phase II randomized study of doxorubicin (A) alternated to docetaxel (T) (ALT) vs sequential administration of 4 cy of t followed by 4 cy of a (seq) as 1st line ct in mbc pts

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From 3/96 to 3/98, 106 pts with untreated MBC were treated with T (100 mg/m^2) and A (75 mg/m^2) on an Alt cy by cy (A.T.A.T.A.T.A.T) or Seq (T.T.T.T.A.A.A.A) basis q3w for a maximun of 8 cy.

Eligibility: meas MBC, age < 75 y, WHO PS 0–2, no prior CT for MBC (prior adj. allowed provided <240 mg/m^2 of prior A) and adequate hemato, renal, hepatic and baseline LVEF. Pts characteristics were well balanced: med age 55 y (29–75), med PS 1 (0–2). Adj. CT: 88% of pts (with anthracycline in 3 pts). Tm charac: Alt/Seq (% pts): visc (82/80), liver (47/54), bone (39/51) and >2 organs (43/40).

Results: med nb of cy is 8 in both arms. Febrile neutropenia and gr 3 inf was observed in 18% Alt and 13% Seq of pts. Except stomatitis (more frequent and more severe with Alt), no other non-hematological severe or gr 3/4 adverse events were observed. With a med. F-up of 14 mo and a med. cum dose of A of 300 mg/m^2, no CHF was observed. Fluid retention was severe in only 1 pt. Activity was similar between Alt/Seq: ORR% 60/67, CR% 2/7, Liver RR% 59/62, Resp Dur wks 47/44, TTP wks 39/38 respectively. As of 3/99 med survival was not yet reached in both arms.

Conclusion: Alt and Seq administration of A and T are safe, feasible and effective regimens. A comparison of Alt or Seq administration of A and T with AT combination is warranted.

1260 ORAL

Randomized open-label phase III multicenter trial comparing TAXOL®/doxorubicin (AT) versus 5-fluorouracil/doxorubicin and cyclophosphamide (FAC) as a first line treatment for patients with metastatic breast cancer

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Objectives: To compare time to progression, response rate, survival safety and quality of life.

Patients: Histologically proven breast carcinoma, previously untreated with chemotherapy for metastatic disease, no prior anthracyclines and/or taxanes, one prior adjuvant chemotherapy allowed if >6 months.

Treatment: Patients received AT: A = 50 mg/m^2 and TAXOL (3-hour infusion at 220 mg/m^2 given 24 hours after doxorubicin) or FAC: F = 500 mg/m^2, A = 50 mg/m^2 and C = 500 mg/m^2 every 3 weeks, for 8 courses. Standard 3-drug premedication was given prior to TAXOL.

Results: From 25Nov96 to 30Mar98, 267 patients were randomized in 29 centers (Central and Eastern Europe, Israel). This randomization was stratified for center, prior adjuvant chemotherapy (AT: 43% – FAC: 44%) and presence of bone metastases (AT: 36% – FAC: 35%). 131 patients were treated with AT and 133 with FAC. The median time to progression (TTP) was significantly superior ($p = 0.034$) for AT: 8.3 months than for FAC: 6.2 months. The overall clinical response rate was 68% in the AT and 55% in the FAC arm ($p = 0.032$) (CR: 19% vs. 8%). Main grade 3–4 toxicities by patient showed: AT is more toxic in terms of neutropenia (89% vs. 65%) but not in terms of febrile neutropenia (8% vs. 5%). Grade 3–4 arthralgia/myalgia (10% vs. 0%), PNS (12% vs. 0%) and diarrhea (2% vs. 0%) was more frequently observed in AT arm. More Grade 3–4 nausea/vomiting (8% vs. 18%) in FAC arm. AT showed delayed CHF in <2% of patients; 1 CHF was observed on-study in FAC.

Conclusion: AT showed a significant advantage in TTP compared to FAC. Preliminary survival data are confirming the efficacy advantage with AT combination but more follow-up is needed.

1261 ORAL

Herceptin (R) improves time to progression following chemotherapy in women with metastatic breast cancer

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Purpose: To assess the efficacy of Herceptin (trastuzumab) in combination with chemotherapy as first-line treatment for women with metastatic breast cancer overexpressing HER2.

Methods: Women were allocated to either doxorubicin/epirubicin plus cyclophosphamide (AC) alone or AC + Herceptin (H) if they had not received previous adjuvant AC. Women who had received previous AC were allocated to paclitaxel (T) or T + H. Doses: Doxorubicin = 60 mg/m^2, epirubicin = 75 mg/m^2, C = 600 mg/m^2, T = 175 mg/m^2 every 3 hours; all chemotherapy was given every 3 weeks for 6 cycles. H = iv 4 mg/kg loading dose then 2 mg/kg every week.

Results: Responses to treatment were confirmed by an independent Response Evaluation Committee. Assessments of response rates and time-to-disease progression (TTP) showed a significant improvement of chemotherapy effect in patients receiving H.

N	RR (%)	TTP (months)	
Chemo	234	32	4.6
Chemo + H	235	49 p = 0.0002	7.6 p = 0.0001
AC	138	43	6.1
AC + H	143	52 p = 0.1038	8.1 p = 0.0003
T	96	16	3.0
T + H	92	42 p < 0.0001	6.9 p = 0.0001

Conclusions: Addition of Herceptin to chemotherapy increased response rate and time-to-disease progression significantly compared with chemotherapy alone.

1262 ORAL

The palliative effect of chemotherapy (CT) in metastatic breast cancer (MBC): Objective tumour response is associated with symptom (Sx) improvement

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Purpose: Providing palliation is a major goal of CT in MBC. However, most trials report response rates and not Sx palliation. This study investigated the association between objective response and improvement in cancer Sx.

Methods: 300 MBC patients (pts) who participated in an NCIC CTG trial of doxorubicin +/− vinorelbine were studied. The 9 most common Sx present at baseline on the EORTC Quality of Life Questionnaire (QLQ-C30) (QoL) and on the toxicity section of case report form (CRF) were selected. Sx improvement, stability and worsening were defined and assessed during therapy using serial QoL and CRF data. The relationship between Sx change and response (CR, PR, SD and PD) was examined using 3 × 3 tables of categorical data and a linear trend test (logistic regression model).

Results: Three baseline Sx (pain, shortness of breath and abnormal mood) showed a significant relationship ($p < 0.05$) between likelihood of improvement and objective response using CRF and QoL data. Constipation, anorexia and nausea showed similar results only in the QoL data. The converse was seen for lethargy. The remaining Sx: cough and insomnia, did not show a trend.

Conclusion: Certain cancer Sx improved in concert with CT related tumor shrinkage in this study. Further work in this area will be useful to determine the surrogate value of objective response in relation to the palliative effect of CT.