to evaluate the activity and safety profile of NVBo as first-line treatment in advanced breast cancer (ABC).

Methods: From 11/97 to 07/00, 64 patients (pts) were entered: median age 63 years, 91% PS 0–1, 30% stage IV disease at diagnosis, and 61% with visceral metastases (lung: 34%, liver: 34%). In 73% of pts, at least 2 organs were involved; prior hormonotherapy (70%) and/or neoadjuvant/adjuvant chemotherapy (31%). NVBo was given at the dose of 60 mg/m^2/week for the first 3 administrations and then increased to 80 mg/m^2 in absence of severe neutropenia defined as one episode of grade 4 or ≥ lepisode of grade 3 neutropenia.

Results: 794 administrations were given (median 9/pt). Relative median dose intensity was 91%. The majority of pts (58/64) underwent dose increase from 60 to 80 mg/m^2. Similarly to NVB i.v, the main toxicity of NVBo was neutropenia (70% of pts and 20% of administrations); grade 4 was seen in 17% of pts and 1.8% of administrations and was complicated in 4 pts (6%). Gastrointestinal events were frequent but of mild to moderate intensity. Grade 3–4 events included nausea (3% of pts), vomiting and diarrhoea in (5%) each. No primary prophylactic antiemetic therapy was recommended. Only one patient experienced one episode of grade3 neuroconstipation. After independent review of efficacy results, 58 patients were evaluable for response (WHO criteria).

	ITT patients (N = 64)	Evaluable patients (N = 58)
CR	4	4
PR	15	14
OR CI 95%	29.7 [18–41]	31 [19–43]
Duration of response (weeks) median	39.2	
PFS (weeks) median [range]	17.4 [2.3–127.6]	

Conclusion: Oral vinorelbine as a single agent is effective. Efficacy results of this study fall in the range of those reported in all the published phase II studies of i.v vinorelbine. The safety profile of oral vinorelbine was qualitatively comparable to the one of NVB i.v. Therefore, oral vinorelbine is a good alternative to i.v vinorelbine in patients with ABC.

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Fluorescence in situ hybridization (FISH) may accurately select patients likely to benefit from herceptin monotherapy

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Background: Herceptin (H) is a humanized anti-HER2 monoclonal antibody and the first oncogene-targeted therapy for HER2-positive patients. HER2 gene amplification and subsequent overexpression of the HER2 protein on the cell surface occurs in approximately 25% of human breast cancers. This alteration is associated with poor prognosis. Patients enrolled in the clinical trials that led to the approval of H were selected using immunohistochemistry (IHC) against the HER2 protein, with those scoring 2+ or 3+ being eligible. Recent data suggest that FISH is an accurate method of choosing patients for H therapy. Methods: A retrospective analysis of FISH status in two trials of H monotherapy was performed: H0650g, in which patients received H as the first non-hormonal treatment for metastatic disease; and H0649g, in which patients received H following one or two chemotherapy regimens for metastatic disease. Results: FISH data were available for 111 patients enrolled in H0650g and 209 of those in H0649g. Of these 82 (73.9%) and 173 (82.8%), respectively, were FISH positive. Outcomes are shown below.

H0650g (first-line monotherapy): RR, 34 vs 7 vs 26% (FISH+ vs FISH- vs IHC+); TTP, 4.9 vs 1.7 vs 3.5 months; overall survival, 24.5 vs 24.4 vs 24.4 months

H0649g (second/third-line monotherapy: RR, 19 vs 0 vs 15% (FISH+ vs FISH- vs IHC+); TTP, 3.2 vs 1.9 vs 3.1 months; overall survival, 14.2 vs 8.8 vs 12.8 months

Conclusions: These results demonstrate that FISH is an accurate method of selecting patients for H therapy. The results further indicate that in optimally selected patients, H is an active therapy for the treatment of HER2-positive breast cancer, particularly when used as first-line therapy for metastatic disease.

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Insulin-like growth factor (IGF) components in postmenopausal metastatic breast cancer (MBC) patient having progressed on tamoxifen: different effect of exemestane (EXE) or megestrol acetate (MA)

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IGF-1 and IGF binding protein (IGFBP)-3 are modifyied in MBC pts receiving hormone therapy. IGF-1, IGF-2 and IGFBP-3 were prospectively evaluated on MBC pts enrolled in a large randomized study of EXE vs MA having progressed on tamoxifen (Kauffman M. et al., JCO 2000). A total of 53 pts were randomized to EXE 25 mg/day (23 evaluable pts) or MA 160 mg/day (28 evaluable pts) and treated until PD. The two groups were well-balanced; all were ER-/PgR-positive. Tumor response and clinical benefit (CR + PR + SD) were 12.5% and 54.2% on EXE and 10.3% and 34.5% on MA. Pts were sampled at baseline, 8 wks, 24 wks and every 12 wks thereafter. Only IGF-1 significantly increased at week 8 and the increase was higher with MA than with EXE. No correlation was found with tumor response. Estrone (E1) and estradiol correlate negatively with IGF-1 (EXE) and with IGF-1 and -2 (MA) ($p < 0.05$). E1-sulphate correlates negatively with IGF-1 (MA) ($p < 0.01$). IGF-1 increases on EXE were lower than on MA. Only the 8 wks data are reported due to pts drop-out for PD.

		Baseline (Geometric mean)	Week 8 (Geometric mean)	Probability (Wilcoxon's test) (Between treatments)	(vs. baseline)
IGF-1	EXE	88	136	<0.05	<0.01
(ng/mL)	MA	85	194		<0.01
IGF-2	EXE	108	109	Not significant (NS)	NS
(ng/mL)	MA	102	107		NS
IGFBP-3	EXE	4.6	5.1	NS	NS
(μg/mL)	MA	4.7	4.9		NS

The present study confirm previous findings indicating an effect of steroidal aromatase inhibitors on the IGF system in MBC pts.

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Fractionated Navelbine and Doxorubicin (NA) as front line chemotherapy in metastatic breast cancer (MBC)

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The activity of Navelbine 25 mg/m2 and doxorubicin 25 mg/m2 [NA] (days 1 and 8 every 21 days for up to 9 cycles) was evaluated in women receiving front line chemotherapy for MBC. All pts had received no prior chemotherapy for metastatic disease and were PS 0-2. Pts with history of brain metastases or significant liver dysfunction were excluded. Prior adjuvant chemotherapy was completed >3 months prior to trial entry and no pt had received < 300 mg/m2 prior anthracycline therapy. All pts had measurable disease. 41 patients were entered on study between May 1999 and May 2000 with a median age of 54 years (range 31-74) and 39 pts received chemotherapy and were assessed for response. 13 pts had received prior adjuvant chemotherapy. The majority of patients presented with multiple sites of disease, with metastases in liver 19pts; lung 9pts; soft tissues 27pts and bone 8pts.

The NA combination was active with 4 CR, 16 PR in 39 pts with a further 12 pts having stable disease for > 3months. Responses were seen at all metastatic sites, median response duration 6.5 mths (range 3.5-11mths). Median survival of 13 months and 17/39 pts remain alive, a minimum of 11 mths after commencing chemotherapy

The treatment was well tolerated in the majority of pts, 200 cycles of therapy administered (median 6 cycles; range 1-9). There were 46 episodes of grade * neutropenia (23% cycles). 45 cycles were delayed but only 6 dose reductions, primarily because of myelosuppression, with day 8 treatment omitted on 7/200 cycles.