in worst pain (P=0.008), and average pain in the last 7 days (P=0.04), interference with general activity (P=0.01) and interference with walking ability (P=0.001). In every case there were significant improvements on treatment in the home setting (P=0.04, P=0.008, P=0.0004, and P=0.003 respectively). Serum creatinine was normal throughout for the majority of participants, with only 4 patients (3%) experiencing an increase in serum creatinine of greater than 44 μmol/l above baseline.

Conclusion: this study demonstrates that Z 4-mg significantly improves QoL and pain scores, particularly when administered to patients at home, and can be given safely in this setting.

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Dose-finding study of the combination of oral idarubicin and oral capecitabine in the treatment of locally advanced or advanced breast cancer

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Introduction: Anthracyclines and 5FU are amongst the most widely used and effective drugs for the treatment of breast cancer. In locally recurrent and metastatic breast cancer response rates of over 70% can be achieved using a schedule of weekly bolus adriamycin and continuous infusional 5FU (Gabra et al. 1996). Many patients however prefer oral chemotherapy, so we have developed an all oral regimen using idarubicin and the oral 5FU pro drug capecitabine.

Materials and Methods: Between June 1999 and July 2003, 30 post menopausal patients were recruited, 17 in the dose finding phase and 13 in the expansion phase. The starting doses were 10 mg/m^2 idarubicin days 1–3 and capecitabine 750 mg/m$^{2\ bd}$ days 1–14, repeated every 21 days.

Doses were escalated as follows; 10/750 (n=6), 10/1000 (n=3), 10/1250 (n=5), 12.5/1000 (n=3), with the expansion phase at 10/1000 (n=13). Patients were evaluated for toxicity with each cycle and for response at cycles 3 and 6. 4 patients remain on treatment. Dose limiting toxicity was defined as either 2 of 6 patients or 2 of 3 patients having the same grade 3 toxicity at a particular dose level.

Results: The median age of patients was 66 (54–76), and the mean number of cycles dispensed was 4.9 (1–12). Two patients were treated for primary breast carcinoma, and the remainder received this regimen as first line chemotherapy for metastatic or locally recurrent disease. All patients had adequate cardiac function assessed by MUGA scanning at entry to the study.

	10/750 (n=6)	10/1000 (n=3)	10/1250 (n=5)	12.5/1000 (n=3)	10/1000 (expansion, n=12)
Episodes of grade 3 or 4 toxicity (neutropenia)	5 (0)	2(1)	5(2)	8(5)	9(5)
Number of dose reductions	0	2	2	1	5
Delays due to toxicity	1	2	7	1	11
Withdrawn for toxicity	2	0	1	1	0

There were three deaths within 4 weeks of receiving trial medication. Two were attributable to progressive disease and one was related to haematological and other treatment related toxicity at the highest dose level. The dose limiting toxicity was neutropenia. Within the dose finding phase there was one complete and 6 partial physician reported responses with a further 3 patients achieving stable disease, giving an objective response rate of 41%. Four patients remain on treatment in the expansion phase, but to date there have been 4 objective responses observed and 4 patients with stable disease within 10 evaluable patients. These were physician reported and will be subject to independent radiological review.

Conclusions: We believe that we have developed a feasible oral cytotoxic regimen for the treatment of primary and advanced breast carcinoma, which shows encouraging evidence of disease activity. The 10/1000 combination requires further evaluation in the phase 2 setting.

References

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Oral Vinorelbine in metastatic breast cancer: Long-term results of 2 multicenter phase II studies

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Navelbine® (NVB) oral is a soft-gelatin capsule for which reliable-dose-equivalence with Navelbine® intravenous (IV) has been demonstrated. Two multicenter, phase II studies (S1 and S2) were conducted to evaluate the activity of NVB oral in the first-line treatment of advanced breast cancer (ABC) using the same inclusion criteria. NVB oral was given at 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 2 episodes of grade 3. Between November 1997 and August 2000, 64 and 72 patients (pts) were enrolled in S1 and S2, respectively. For both studies median age was 63 years; 61% of pts in S1 and 47% in S2 had visceral lesions. The majority of pts underwent dose increase from 60 to 80 mg/m^2 (95% for S1, 86% for S2). Median number of administrations were 9 and 10, respectively. Main efficacy results are displayed in table 1.

Table 1

	RR* all pts	RR* evaluable pts	Median PFS**	Median survival
S1	30%	31%	4.2 mo	24 mo
S2	27%	30%	4.6 mo	21 mo

* RR, Response Rate; **Progression-free survival.

Safety results from the 2 studies were pooled. Main dose-limiting toxicity was neutropenia with 42% of pts with grade 3–4 and 4% with febrile neutropenia. Non haematologic toxicities included nausea (8% of pts with grade 3–4), vomiting (8% with grade 3–4), diarrhea (7% with grade 3) and constipation (1% with grade 3). Nausea and vomiting are easily controlled by prophylactic use of antiemetics, preferably oral setrons. No toxic death was reported.

In conclusion, NVB oral gave consistent results in two independent studies. It has shown the same efficacy and safety profile as NVB IV with the advantages of convenience and lack of venous toxicity of oral chemotherapy.

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Weekly docetaxel and trastuzumab for her-2-overexpressing metastatic breast cancer: efficacy and correlation with biological markers in a phase II, multicenter study

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Purpose: 1) To evaluate the efficacy and safety of weekly docetaxel and trastuzumab for patients with HER-2 overexpressing metastatic breast cancer. 2) To analyze correlations between response and the expression of biological markers.

Patients and Methods: Thirty-five women with HER-2 overexpressing metastatic breast cancer were enrolled in the study. Eligible patients received Trastuzumab 4 mg/kg day 1 before the start of the first cycle followed by docetaxel (40 mg/m^2) and trastuzumab (2 mg/kg) weekly for three weeks. The pretreatment expression of p53, Bcl-2, Caspase-3, MAP Kinase, and R-ras in 18 cases were evaluated by immuno- histochemical staining.

Results: 1) The overall response rate was 61.8% (95% CI: 44–79) [complete and partial response, 6 (18%) and 15 (44%), respectively]. The median time to failure was 154 days (range, 28 to 616 days). 2) The median number of cycles administered was four (range, 1 to 8). The median delivered dose-intensity for docetaxel was 27 mg/m^2 (range, 19 to 30), which is equal to a median relative dose-intensity of 90%. 3) Grade 3/4 toxicities (NCI-CTCver.2) were neutropenia 9 pts (26%), anorexia 1 pts (3%), fatigue 1 pts (3%), diarrhea 1 pts (3%), stomatitis 1 pts (3%). 17 pts (49%) showed Grade 2 nail changes and 7 pts stopped treatment by this adverse events. 4) The pretreatment expression of p53, Bcl-2, Caspase-3, MAP kinase, and R-ras was unlikely to predict