Methods: Between August 2003 and April 2006, 40 patients (pts) with HER2+ MBC (IHC 3+ or FISH+) have been included in the study. Pts received Trastuzumab (loading dose of 4 mg/kg/wk and 2 mg/kg/d following wks), Paclitaxel (80 mg/m^2) and Carboplatin (AUC 2) all given weekly $\times$ 3 followed by 1 week of rest. Treatment was given until disease progression or unacceptable toxicity.

Results: 40 pts had baseline data available. Median age was 54 yrs (range 29−75). 38 (95%) pts received prior adjuvant or neoadjuvant treatment. 11 (27.5%) pts have received one prior CT line for metastatic disease. 87.5% pts had PS 0 or 1 at study entry. Disease sites were liver 16 (40%), bone 12 (30%), lymph nodes 13 (32.5%) and lung 8 (20%). 19 (47.5%) had >2 lesions. 97.5% had measurable disease.

36 patients have been evaluated for response: 11 CR (31%, 95% CI: 15−46%), 11 PR (31%, 15−36%), 9 SD (25%, 9−36%), 5 PD (14%, 2−26%) and 4 NE resulting in an ORR of 61% (95% CI: 45−77%) and tumor growth control rate (RR+SD) of 86% of patients (95% CI: 75−97%). Median TTP was 12.1 mo (95% CI: 8.8−19.9 mo) and median duration of response have not been reached yet. For a time of observation of 41.8 mo, the median OS is 33.1 mo (95% CI: 18.9−. . .). At a median follow-up of 39.4 mo from the inclusion, 14 pts (35%) developed CNS metastases: 9 pts (22.5%) as first progression site and 5 pts (12.5%) as later progression. For CNS met. pts TTP was 17.3 mo (r 2.2−44.2), and OS was 27.7 mo (r 12−48).

37 patients have received 194 cycles with a median of 5 cycles. Grade 3−4 toxicities/pts were: 3 (7.5%) anaemia, 2 (5%) leucopenia, 8 (20%) neutropenia, 1 (2.5%) febrile neutropenia, 1 (2.5%) trombopenia, 2 (5%) asthenia, 2 (5%) diarrhea, 3 (7.5%) nausea, 2 (5%) vomiting, 3 (7.5%) mucositis.

Conclusions: This interim analysis shows an interesting activity with this regimen. One week of rest may be of better convenience for the patient and hospital but also may improve the tolerability profile and efficacy of the combination. We observed a incidence of CNS metastases similar to that reported in other trials, but the survival is longer than in patients unselected for Her-2 status. The better control of extracranial disease reported in our experience is probably the cause of the longer survival of these CNS metastatic patients. Further results would be available for presentation.

411 Poster

Metronomic oral vinorelbine and temozolomide, after whole brain radiotherapy, for the treatment of breast cancer patients with brain metastasis. A phase II study

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Background: The incidence of Central Nervous system (CNS) metastases has been reported to be 15−25% in patients with breast cancer. Whole Brain Radiotherapy (WBRT) remains the mainstay of therapy for brain metastasis of solid tumours not amenable to surgical resection. Temozolamide (TMZ) is a new orally administered imidazo-tetrazine with proven activity in Brain metastasis. Vinorelbine The recently introduced oral form of this vinca alkaloid derivative, Vinorelbine, has disclosed new and useful perspectives particularly for elderly patients.

Methods: Patients with breast cancer and newly diagnosed, inoperable, brain metastases (BM) were eligible. We have treated 19 consecutive patients (mean age: 55.2 + 22.4 yrs; median age: 57.9 yrs) affected by brain metastases with WBRT at 3 Gy/day administered over a two-week period (on wks 1–2), total dose 30 Gy, and an induction with TMZ 75 mg/m^2/day during this period, followed by 4 weeks off-therapy and subsequent original schedule with TMZ administration at 75 mg/m^2 on days 1–21 every and oral Vinorelbine (VNR) 70 mg/m^2 fractionated in days 1, 3 and 5, one week on-one week off, every four weeks up to twelve additional cycles. Pts who received at least one cycle of TMZ and VNR were assessable for response.

Results: All patients were subjected to the induction therapy and 86 cycles were performed, mean cycles 4.7. Two grade three, twelve grade II ad ten grade I neutropenia (CTC), five grade II anemia, seven grade I and four grade II thrombocytopenia and nine grade I alopecia were recorded. Fourteen grade I and 7grade III, nausea and vomiting were observed, moreover, liver or renal toxicity were never recorded in our series being the schedule well tolerated in all patients. two CR (10%), and 8 PRs (42%) were recorded while a clinical benefit was achieved in other four patients (21%). The Objective Response rate was 52% (C.I. 42.7−64.9%), while the disease control rate was 73% (C.I. 61.7−82.4%). Nine still alive patients, who achieved a PR and a SD, had an overall survival between 19 and 9 months, respectively. At the present, in our series, overall survival was 59% at 1 year. Patients continue to be followed to evaluate long term effects of the treatment. Our study found a high level of satisfaction for QoL.

Conclusions: These preliminary results show that some of the pts who received complete treatment plan could achieve prolonged disease control and survival. The schedule was safe and well tolerated (also in old pts.) and has suggested an encouraging activity in brain metastases from breast cancer. Final data analysis will be presented.

412 Poster

All-oral vinorelbine (NVBo) and capecitabine (X) combination for chemotherapy-naïve HER2-negative metastatic breast cancer (MBC) patients: efficacy and safety in an international phase II study

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Background: NVBo and X have shown single-agent activity in MBC and combination of these two oral agents with non-overlapping key toxicities is logical. We report the latest efficacy and safety data from an international phase II study of all-oral NVBo plus X.

Methods: Eligible patients had measurable HER2-negative MBC, had received no prior chemotherapy for MBC, had relapsed greater than or equal to 6 months after completing (neo)adjuvant chemotherapy and had Karnofsky PS greater than or equal to 70%. Patients received 3-weekly cycles of NVBo 80 mg/m^2 (first cycle at 60 mg/m^2, escalating in the absence of G3/4 neutropenia) d1 and d8 in combination with X 1000 (750 if greater than or equal to 65 years) mg/m^2 twice daily d1−14. Treatment was continued until progression or unacceptable toxicity. The primary endpoint was response rate (RR) by RECIST.

Results: Baseline characteristics of the 55 enrolled pts (one not treated) were: median age 58.5 years (41% greater than or equal to 65); chemotherapy for early breast cancer 63% (predominantly anthracyclines, 85% with a taxane in 18%); prior hormone therapy 76%; visceral involvement 78% greater than or equal to 3 metastatic sites 46%. Patients received a median of 7 cycles (range 1–45). Median relative dose intensity was 87% for both agents and 94% received the escalated NVBo dose. G3/4 NCI CTC v2 adverse events in >5% of patients were: leucopenia 28%, neutropenia 49%, vomiting 9%, stomatitis 7%, fatigue 7%, febrile neutropenia 6%, infection with neutropenia 6%. The RR in 47 evaluable pts was 51% (95% CI: 36−66), including one complete response (2%). Stable disease (SD) was reported in an additional 30%. The clinical benefit rate (CR + PR + SD for >6 months) was 64%. After median follow-up of 21.1 months, median progression-free survival is 8.4 months. Median overall survival has not been reached.

Conclusions: The all-oral combination of NVBo and X is an effective and well-tolerated first-line therapy for MBC. Treatment was continued for up to 45 cycles. The efficacy of this combination with the added benefit of oral administration has led to initiation of a randomised trial versus i.v. combinations in the first-line setting.

413 Poster

Is HER-2 over expression associated with brain metastases in Chinese breast cancer patients?

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Background: Brain metastases occur in 10−15% of metastatic breast cancer patients and are associated with poor prognosis. This study aims to identify tumor characteristics of the primary breast cancer which are related to brain metastases in Hong Kong Chinese patients.

Material and Methods: A retrospective study of patients with invasive breast cancer receiving treatment in a university hospital from January 2001 to December 2005 was performed. Clinico-pathological factors of those patients with brain metastases were compared with those without. HER-2 over expression was confirmed either by 3+ protein over expression using immunohistochemistry or by HER-2 gene amplification using fluorescence in situ hybridization.

Results: 787 patients with invasive breast cancer were treated during the study period. 30 patients were found to have distant metastases to brain. The median age of the patients at the diagnosis of brain metastases was