

**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<sup>2</sup>) 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%) thrombopenia, 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 an 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.

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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. Temozolomide (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  $\pm$  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<sup>2</sup>/day during this period, followed by 4 weeks off-therapy and subsequent original schedule with TMZ administration at 75 mg/m<sup>2</sup> on days 1–21 every and oral Vinorelbine (VNR) 70 mg/m<sup>2</sup> 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 7 grade 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.

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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<sup>2</sup> (first cycle at 60 mg/m<sup>2</sup>, 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<sup>2</sup> 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.

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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

53 years (range 28–80 years). Four patients (13.3%) underwent resection of brain metastases, twenty-three patients (76.7%) received whole-brain radiation therapy, and six patients (20%) had gamma-knife surgery. The median overall survival time was 8 months (95% CI, 6–10 months). Patients with brain metastases had more breast tumors of larger size ( $p = 0.000$ ), positive lymph node status ( $p = 0.049$ ), higher histological grade ( $p = 0.001$ ), higher rate of negative estrogen receptors ( $p = 0.023$ ) and higher rate of HER2 over-expression ( $p = 0.000$ ). By multivariate analysis, larger tumor size, negative estrogen receptor status and HER2 over-expression were found to be independent significant factors associated with brain metastases.

**Conclusions:** Primary breast cancers which metastasize to the brain in Chinese patients are usually estrogen receptor negative and HER2 over expressing. This finding is consistent with those observed in Western literatures. Targeted therapies towards HER2 over-expressed tumors which can cross the blood brain barrier are needed to treat breast cancer patients with brain metastases effectively.

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Poster

#### Skeletal-related event (SRE) history, bone metastasis location and number affect SRE risk and patient survival in metastatic breast cancer

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**Background:** The majority of patients with advanced breast cancer develop bone metastases. Survival in these patients ranges from 2 to 3 years. The prognostic potential of certain skeletal health indices measured during bisphosphonate therapy have not been systematically investigated. We conducted a retrospective analysis of data from a pamidronate-controlled trial of zoledronic acid in patients with bone metastases from breast cancer (Rosen LS, et al. *Cancer* 2003;98:1735–1744) to determine the association between patient SRE history, and lesion number and location on SRE risk and survival.

**Material and Methods:** Only patients treated with zoledronic acid who had lesion site and number, SRE history, and bone pain data were included in this analysis. Univariate analyses were used to assess risk ratios (RR) for time to first SRE and death at baseline ( $n = 664$ ), 6 ( $n = 553$ ) and 12 months ( $n = 435$ ). SREs included pathologic fracture, spinal cord compression, radiotherapy or surgery to bone.

**Results:** In patients who had a prior SRE at baseline, the risk of a subsequent SRE was increased 2.15-fold ( $P < 0.0001$ ) compared with patients who had not experienced a prior SRE. Patients with prior SREs at 6 and 12 months also had a higher risk of subsequent SREs ( $RR = 2.305$ ,  $P < 0.0001$ ;  $RR = 1.88$ ,  $P = 0.016$ , respectively). Similarly, patients with  $\geq 4$  bone lesions at each time point assessed had a significantly increased risk of experiencing another SRE ( $P < 0.001$  for all). Lesions in weight-bearing bones did not significantly increase the risk of subsequent SREs. At baseline, patients with a prior SRE had a significantly increased risk of death compared with patients without prior SREs ( $RR = 1.361$ ,  $P = 0.0083$ ), and the risk was also higher at 6 months ( $RR = 1.543$ ,  $P = 0.0029$ ) and 12 months ( $RR = 1.455$ ,  $P = 0.0481$ ). Patients with  $\geq 4$  bone lesions at baseline, 6 and 12 months had a significantly higher risk of death ( $RR = 1.372$ , 1.666, 1.758, respectively;  $P < 0.006$  for all). At 12 months, patients who had  $\geq 1$  lesion in a weight bearing bone had a 44% increased risk of death that was not statistically significant.

**Conclusions:** The disease parameters prior SRE and  $\geq 4$  bone lesions significantly increased the risk of subsequent SREs and death when assessed at baseline, 6 and 12 months. Patients with  $\geq 1$  lesion in weight-bearing bones only had an increased risk of death without affecting their risk of subsequent SREs. Multivariate analyses to place these parameters in context with other prognostic variable are under way.

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Poster

#### Retrospective analysis of chemotherapy choices and overall survival according to treatment in 96 patients >75 years old with metastatic breast cancer

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**Background:** The optimal treatment for patients (pts) >75 years of age with metastatic breast cancer (MBC) is unclear and shows wide variation between clinics and countries.

**Methods:** We analysed all pts treated from 1<sup>st</sup> January 2000 for MBC at the Institut Bergonié, Bordeaux, France. To be eligible, pts must have received their first line of chemotherapy at age >75 years.

**Results:** The analysis includes 96 pts (median age 78, range 75–91). Seven pts (7%) were  $\geq 85$  years and 34 (35%) were  $\geq 80$  years when they received their first chemotherapy for MBC. First-line chemotherapy consisted of capecitabine in 53 pts (55%), vinorelbine in 21 (22%), combined with gemcitabine in 2 pts (2%), FEC<sub>50</sub> in 12 (13%), docetaxel in 6 (6%), liposomal doxorubicin in 2 (2%), mitoxantrone in 1 (1%) and 'other' in 1 (1%). Choice of chemotherapy was not age dependent: median age was 78.4 years in the subgroup receiving capecitabine and 77.0 and 77.3 years in the subgroups receiving vinorelbine and FEC<sub>50</sub>, respectively. In our clinic, capecitabine was first used in January 2002 and was given in 53 of 67 patients (79%) treated thereafter. As of January 2008, median overall survival (OS) from the start of chemotherapy was 14.0 months (95% CI: 11.3–16.7). Survival rates at 3 months, 1 year and 2 years were 82.2%  $\pm$  4.1%, 56.1%  $\pm$  5.1%, and 25.0%  $\pm$  4.6%, respectively. Subanalysis according to age showed median OS of 15.2 months  $\pm$  3.4 (SE) in pts aged 75–76 ( $n = 33$ ), 10.1 months  $\pm$  2.1 in pts aged 77–79 ( $n = 29$ ) and 13.3 months  $\pm$  2.0 in pts aged  $\geq 80$  years ( $n = 34$ ). Median OS was longest in pts receiving capecitabine (15.1 months  $\pm$  2.6, vs 10.0 months  $\pm$  3.2 in pts receiving other chemotherapy).

**Conclusions:** To our knowledge, there are no published data on efficacy outcomes with chemotherapy use in MBC pts >75 years. In the early part of this decade, various chemotherapy regimens were used, with vinorelbine and FEC among the most commonly administered. We now prefer capecitabine for a large majority of this pt population, based on high efficacy and good tolerability. Our observations support the use of capecitabine as first-line treatment in this setting, with many pts deriving substantial benefit from this therapy (median OS of 15.1 months).

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Poster

#### Randomized comparisons of weekly versus every-3-week nab-paclitaxel in patients with metastatic breast cancer

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**Background:** Nanoparticle albumin-bound (nab)-paclitaxel is a novel taxane that has demonstrated nearly double the overall response rate (ORR) in patients with metastatic breast cancer (MBC) compared with solvent-based paclitaxel. The current analysis compares the safety and efficacy of 2 different dosing schedules of nab-paclitaxel from phase II and phase III trials in patients with MBC.

**Materials and Methods:** This is a subset analysis of the nab-paclitaxel arms of 2 large randomized phase II (CA-024) and III (CA-012; Gradishar et al. *J Clin Oncol*. 2005;23:7794–7803) trials that compared nab-paclitaxel with either solvent-based paclitaxel or docetaxel in patients with MBC. Patients received nab-paclitaxel 260 mg/m<sup>2</sup> intravenously (IV) every 3 weeks (q3w) in the phase III trial and 300 mg/m<sup>2</sup> IV q3w, 100 mg/m<sup>2</sup> IV weekly 3 out of 4 (qw 3/4), or 150 mg/m<sup>2</sup> IV qw 3/4 in the phase II trial. All doses were administered over 30 minutes without corticosteroid or antihistamine premedication or special tubing sets.

**Results:** See the table.

	Every 3 weeks		Weekly	
	300 mg/m <sup>2</sup> (n = 76)	260 mg/m <sup>2</sup> (n = 229)	150 mg/m <sup>2</sup> (n = 74)	100 mg/m <sup>2</sup> (n = 76)
Received as 1st-line therapy, %	100	43	100	100
ORR, %	46	33	74	63
mPFS, months	10.9	5.2	14.6	7.5
mOS, months	NA	14.9	NA	NA
Grade 4 neutropenia, %*	5	9	9	5
Grade 3 PN, %	17	10	14	8

Data from study CA-012 were previously reported (Gradishar et al. *J Clin Oncol*. 2005; 23:7794–7803).

ORR = Overall response rate; mPFS = Median progression-free survival; mOS = Median overall survival; NA = Not available because data is not yet mature for phase II study.

\*Grade 4 neutropenia based on central laboratory data.

**Conclusions:** Nab-paclitaxel demonstrated efficacy and was well tolerated regardless of dose regimen. Grade 4 neutropenia and grade 3 sensory neuropathy were similar in the nab paclitaxel weekly groups compared with the nab-paclitaxel q3w groups. Because of the superior