treated with trastuzumab and chemotherapy. Clinical trials are indicated to evaluate:1) if an active surveillance in HER2-overexpressing MBC pts (by TC or MRI) may be beneficial for early CNS metastases diagnosis and treatment; 2) or if there is indication to prophylactic cranial irradiation (PCI) in a population at high risk of developing brain metastases.

413 POSTER

A multicenter Phase II study of Epirubicin (E) with low-dose Herceptin (LD-H) as a first line treatment in HER-2 overexpressing metastatic breast cancer (MBC): Preliminary results

M. De Tursi[1], C. Carella[1], E. Ricevuto[2], P. Marchetti[2], A. Gennari[3], C. Orlandini[3], A. Frassoldati[4], P. Conte[4], S. Iacobelli[1]. [1]*Medical Oncology – University of Chieti, Dept. of Oncology and Neurosciences, Chieti, Italy;* [2]*Medical Oncology – University of L'Aquila, Dept. of Oncology, L'Aquila, Italy;* [3]*Medical Oncology – University of Pisa, Dept. of Oncology, Pisa, Italy;* [4]*Medical Oncology – University of Modena and Reggio Emilia, Dept. of Oncology, Modena, Italy*

Background: The combination of Doxorubicin and Herceptin (H) proved to be an effective regimen in advanced breast cancer, although it was associated with an increased risk of cardiotoxicity. The aim of this study was to evaluate the activity and cardiac safety of the combination of Epirubicin (E) with low-dose Herceptin (LD-H).
Material and methods: This was a two step study: In the first step, H was given at a loading dose of 2 mg/Kg on day 1, followed by 1 mg/Kg weekly; in the second step ($\geqslant$ 12 objective responses/21 pts), the dose of H was increased to 2 mg/kg weekly. E was administered at 90 mg/m^2 on day 1 every 3 weeks. After 6–8 courses of this combination, H was administered as a single agent for a maximum of 52 weeks. To assess cardiotoxicity, pts were evaluated for the Left Ventricular Ejection Fraction (LVEF) at baseline, every two cycles during E and LD-H, and every three months during LD-H alone. Either ultrasonography or angioscintigraphy were used. Cardiotoxicity was defined as the appearance of signs or symptoms of congestive heart failure in $\leqslant$10% of pts at an E dose of 720 mg/m^2 or in $\leqslant$20% of pts at an E dose > 720 <1000 mg/m^2.
Results: Twenty-one pts entered the first step: median age was 55 years (41–70 years), hormonal status was positive in 9 pts and negative in 10. Eight pts had received prior adjuvant anthracyclines, and 8 pts prior endocrine therapy. The majority of pts had > 2 organ sites of involvement with visceral lung metastases predominating. A median of 6 cycles (range 1–18) was administered with 134 cycles evaluable for toxicity. The regimen was well tolerated, with grade 3/4 neutropenia, alopecia, and thrombocytopenia occurring in 55%, 25% and 10% of the pts, respectively. Six episodes of cardiotoxicity were observed (an asymptomatic decrease in LVEF *15% in 4 pts and an asymptomatic decline of LVEF at $\leqslant$50% in 2 pts). At the time of analysis, 12 (57%) pts achieved a partial response, 6 (%) had stable disease, and 3 (%) had progressive disease. The median time to progression was 9.8 months (95%CI: 5. 5–14.1) and the median overall survival was not reached.
Conclusions: These preliminary results show that the combination of E+LD-H possesses good antitumor activity, with limited cardiotoxicity. The Protocol Committee recommended to enter the second step of the study, maintaining the dose of H at 1 mg/Kg weekly. Accrual is continuing; an update will be presented at the meeting.

414 POSTER

Final results of the HERMINE cohort: a retrospective and prospective, longitudinal French cohort study of 623 metastatic breast cancer women treated by trastuzumab

J. Extra[1], E.C. Antoine[2], A. Vincent-Salomon[1], M.C. Le Deley[3], L. Bergougnoux[4], B. Remblier[4], B. Vasseur[4], M. Namer[5]. [1]*Institut Curie, Oncologie Médicale, Paris, France;* [2]*Clinique Hartmann, Oncologie Médicale, Neuilly-sur-seine, France;* [3]*Institut Gustave Roussy, Oncologie Médicale, Villejuif, France;* [4]*Roche, Oncologie Médicale, Neuilly-sur-Seine, France;* [5]*Centre Antoine Lacassagne, Oncologie Médicale, Nice, France*

Background: The efficacy and safety of trastuzumab (T) in combination with taxanes have been documented in clinical trials of HER2-positive metastatic breast cancer (MBC), particularly in terms of overall survival (OS) and time to progression (TTP) in first-line therapy. The aim of the study was to understand treatment use and outcomes in a large patient population under real-life conditions.
Methods: HERMINE is a longitudinal, observational study by 102 oncologists in France. Eligible patients (pts) $\geqslant$ 18 yrs all had MBC and started T treatment in 2002. Initial data were collected retrospectively (ESMO 2004), with a *2-year follow-up. All data were collected from patient files and reviewed by an independent scientific committee. Study endpoints included duration of T treatment, TTP, OS and cardiac safety.
Results: A total of 623 of 643 pts were analysed with a median follow-up of 23 months. Pts had a median age of 56 years (27–85 years), with median time from first diagnosis of 4.5 years and median disease-free interval of 2.0 years; 20% had MBC at first diagnosis, 71% had visceral metastases and 23% had past cardiac history. Tumour characteristics are as follows: ductal carcinoma = 91%, HER2-positive (IHC 3+) = 93%; SBR III = 56%; ER-positive and/or PR-positive = 6%; ER and PR-positive = 33%. Pts previously had surgery (88%), radiotherapy (82%), chemotherapy (90%) and/or hormonal therapy (58%). T treatment was once-weekly (89%), in combination with other treatment (94%) (paclitaxel = 61%, vinorelbine = 35%, docetaxel = 25%, capecitabine = 9%, or others). There were 19 heart failures (3% of pts) but no death was related to T adverse events. Table 1 presents the median T treatment duration, TTP and OS, according to T treatment lines (Kaplan-Meier method).

Table 1: Comparison of median T treatment duration, TTP and OS

T treatment (lines)	Median [95%CI] T treatment duration (months)*	Median [95%CI] TTP (months)*	Median [95%CI] OS (months)*
1st line (n = 221, 37%)	16.2 [13.2; 18.6]	10.3 [9.3; 12.5]	30.4 [25.4]
2nd line (n = 138, 23%)	15.9 [13.2; 19.4]	9.0 [7.2; 10.6]	27.2 [22.7; 33.0]
$\geqslant$3rd line (n = 243, 40%)	8.9 [7.3; 12.2]	6.3 [5.6; 7.8]	23.3 [20.3; 26.2]
All (n = 623)	13.4 [11.1; 15.5]	8.6 [7.7; 9.3]	26.0 [23.4; 29.0]

* $p < 0.05$

Conclusion: Two-year results confirm that heart failure frequency is similar to results of previous pivotal trials. Results confirm the efficacy data from the M77001 trial in terms of TTP (11.7 months) and OS (31.2 months).

References

[1] ESMO abstract 109PD, 2004.

415 POSTER

Biological and clinical concordance during chemotherapy in metastatic breast cancer

M. Ruiz-Lopez[1], L. Tejedor-Cabrera[1], C. Iradi-Martinez[2]. [1]*Hospital Punta de Europa, Oncology, Algeciras, Spain;* [2]*Hospital Punta de Europa, Clin Chem, Algeciras, Spain*

Background: Frequently in clinical practice, the anatomic standard response evaluation to chemotherapy (CT) becomes difficult, mainly due to cases of non measurable disease and limitations in imaging availability. The usefulness of circulating tumour markers (CTM) in monitoring CT in Metastatic Breast Cancer (MBC) remains under investigation. We try to analyse the biological (bio) and clinical (clin) concordance during CT in MBC.
Material and methods: In 106 consecutive courses of different schedules of CT given along 3 years to 55 patients with progressive MBC, we conducted a prospective trial analysing 4 CTM – oncofetal, 2 mucin related and cytokeratin (CK) – every 3 weeks before CT infusions and performed CTM concentration / time curves. Clinical responses (Cl R) were measured every 2 months according to UICC criteria (measurable disease, 84% of the courses) and Eagan criteria (evaluable disease, 16%). Bio kinetic change has been defined as a lineal slope that includes 2 early and consecutive changes of at least 25% of CTM start value. The analysis covered 604 cycles, 405 curves and 2417 marker determinations. Statistical was performed by SPSS 11.
Results: The sensibilities of CTM at start values of treatment were:
CEA: 72/106 (67.9%)
CA 15.3: 87/106 (82.1%)
CA 549: 76/94 (80.9%)
TPA: 82/97 (84.5%)
Clinical responses were: CR: 15; PR: 41; SD: 25; PD: 21; NE: 4. In CTM expressing diseases, 3 biological patterns during CT can be detected corresponding to directional possibilities: progressive elevation (Pbio), progressive download (Rbio) and stabilization (without bio kinetic criteria of change (Sbio). Considering 2 types of bio responses, progression (Pbio) versus biological control (Cbio = Rbio+Sbio), the cross matching with corresponding clinical responses, i.e., clinical progression (Pclin) versus clinical control (Cclin = CR+PR+SD) shows an excellent concordance between clin and bio behaviours for any expressing marker: 97% for CEA; 97.5% for CA 15.3; 95.7% for CA 549 and 98.7% for TPA(CK 18–19), Tables shows results of circulating CA 15.3 and Cytokeratin 18–19 (TPA). Tables showing other CTM results, as patterns of curves, will be presented as a poster at the meeting.

Cross Tables of 2 × 2 clin/bio responses

	CA15.3			TPA		
	Cbio	Pbio	Total	Cbio	Pbio	Total
Cclin	63	1	64	61	1	62
Pclin	1	14	15		13	13
Total	64	15	79	61	14	75

Mucin (CA 15.3): Chi^2 Pearson = 66.53, P = 0.000 Concordance+ = 77/79 matches (97.5%) CK 18–19 (TPA): Chi^2 Pearson = 68.52, P = 0.000 Concordance+ = 74/75 matches (98.7%)
Conclusions: In CTM expressing tumours and taking into account simple application kinetics criteria, the analysis of CTM before CT infusion and its concentration / time curves, behaves as an excellent and dynamic surrogate to anatomical criteria in the evaluation of the disease control during CT in MBC.

416 POSTER

Do very young breast cancer patients have worse outcomes in Korea?

J.K. Kim, B.S. Kwak, S.H. Ahn, H.J. Kim, J.S. Lee, S.J. Hong, B.H. Son. *University of Ulsan, College of Medicine, Asan Med, surgery, Seoul, Korea*

Background: The Korean women with breast cancer is younger than white women. This study was designed to compare the clinicopathologic differences and prognosis in very young patients and less young patients among premenopausal Korean women with breast cancer.
Methods: Of breast cancer patients treated at the Asan Medical Center in Seoul, Korea, from 1989 to 2002, 381 patients (9.6% of all breast cancer patients) were younger than 35 years (the "very young" group) and 2320 ranged in age from 35 to 50 years (the "less young" group). In this study, the clinicopathologic factors and survival rates of these 2 groups were compared retrospectively.
Results: The 5-year survival rate was 81.0% in the very young group and 89.1% in the less young group($p < 0.001$). However, on a stage-by-stage basis, No significant difference in survival was seen between the groups. The very young group with lymph node metastasis demonstrated a poorer 5-year survival rate (69.9% vs. 82.7%, $p = 0.0063$) and disease-free survival rate (58.1% vs. 74.1%, $p < 0.0001$) than did their older counterparts. The very young group had more advanced-stage disease ($p < 0.001$), higher T-stage disease ($p = 0.001$) and more positive lymph node ($p = 0.024$) than did their older counterparts and higher percentages of estrogen-receptor negative tumors (48.2% vs. 42.1%, $p = 0.047$), progesterone-receptor negative tumors (53.5% vs. 44.1%, $p = 0.002$) and grade-3 histology (52.1% vs. 43.5%, $p = 0.011$). In patients with an endocrine-responsive tumor, those in the very young experienced a significantly worse outcome than did those in the less young group(86.3% vs. 93.9%, $p = 0.0108$ in ER(+); 85.9% vs. 94.9%, $p = 0.0094$ in PgR(+)).
Conclusions: The Korean women younger than 35 years with breast cancer have a worse prognosis, a higher rate of recurrence, a later stage at diagnosis, and more aggressive biologic factors than older premenopausal patients. An age of younger than 35 years was an independent predictor for recurrence. Our results show that physicians must be aware of the consequences of breast cancer in younger patients and must recognize that (especially in node-positive patients) a therapeutic strategy more aggressive that that used in older patients may be required to optimize outcome.

417 POSTER

Maintenance hormone therapy with letrozole after first-line chemotherapy in postmenopausal patients with hormone receptor-positive metastatic breast cancer

M. Ruiz Borrego[1], J. De la Haba[2], S. Morales[3], M. Ramos[4], A. Velasco[5], M. Mendez[6], F. Carabantes[7], A. Barnadas[8], M. Garcia[9], J.A. Moreno[1]. *[1]Virgen del Rocio Hospital, Dept. of Oncology, Sevilla, Spain; [2]Reina Sofia Hospital, Dept. of Oncology, Cordoba, Spain; [3]Arnau de Vilanova Hospital, Dept. of Oncology, Lleida, Spain; [4]Oncological Center of Galicia, Dept. of Oncology, La Coruña, Spain; [5]La Princesa Hospital, Dept. of Oncology, Madrid, Spain; [6]Mostoles Hospital, Dept. of Oncology, Mostoles, Spain; [7]Carlos Haya Hospital, Dept. of Oncology, Malaga, Spain; [8]Germans Trias i Pujol Universitary Hospital, Dept. of Oncology, Badalona, Spain; [9]Ciudad Real Hospital, Dept. of Oncology, Ciudad Real, Spain*

Background: Metastatic breast cancer treatment aims to obtain a good control of the disease by optimizing the available therapeutic approaches. Maintenance chemotherapy beyond a response is often associated with toxic side effects and many patients prefer to discontinue such treatment. In this study we assessed the efficacy for letrozole (Femara®) as a maintenance hormonal therapy after chemotherapy in post-menopausal metastatic breast cancer hormone receptor-positive patients.
Material and methods: Multicentre prospective trial. Women who received standard first-line chemotherapy for at least 3 months and had a complete response (CR), partial response (PR) or stable disease (SD), were then treated with letrozole p.o. 2.5 mg/day until progression disease or unacceptable toxicity. The main endpoint of the study was time to progression (TTP). Secondary endpoints were safety and response rate conversion. The data are presented with a median range of follow-up of 17 months.
Results: From June 2001 to August 2003 142 patients were included in the study. Median age: 60 years (36–81). Prior treatments: neo/adjuvant chemotherapy: 100%, neo/adjuvant hormone therapy: 46%, surgery: 80% and radiotherapy: 41%. 103 patients were assessed for efficacy and 124 for toxicity. Response obtained after chemotherapy: 27% CR, 28% PR and 45% presented SD. The median TTP was 19 months from starting with letrozole. A trend to a longer TTP in patients with CR and better performance status (ECOG) has been observed. A conversion response rate from SD to PR of 4.3% and from PR to CR of 12.5% was obtained from switching from chemotherapy to letrozole. The median overall survival (OS) was 37 months. Letrozole was well tolerated. The most frequent side effects associated with letrozole were: arthralgia, bone pain and headache.
Conclusions: Maintenance therapy with letrozole after chemotherapy was associated to a prolonged TTP and overall survival and improved the overall response. These results support the feasibility of switching patients to letrozole after achieving disease control with chemotherapy in postmenopausal women with hormone receptor positive advanced breast cancer.

418 POSTER

Cost-effectiveness of zoledronic acid vs. other bisphosphonate agents for the prevention of bone complications in breast cancer: an application to Canada

K. El Ouagari[1], M. Botteman[2], M. Aapro[3], J. Hay[4], J. Stephens[2], J.P. Brandman[5]. *[1]Novartis Pharma, Health Policy & Market Access, Dorval, Canada; [2]Pharmerit North America, Bethesda, USA; [3]Clinique De Genolier, Switzerland; [4]USC School Of Pharmacy, Los Angeles, USA; [5]Novartis Pharma, Marketing-Health Economics, East Hanover, USA*

Background: Bisphosphonate therapies have been approved and recommended for the prevention of bone complications in patients with breast cancer. However, these agents differ in terms of efficacy, administration time, and costs. An economic analysis was conducted to assess the relative cost effectiveness of various bisphosphonates for the prevention of bone complications in Canadian breast cancer patients with metastatic bone.
Methods: A Markov model was developed to estimate and compare the costs and quality adjusted life year (QALY) of no therapy (PL), IV pamidronate (PA), IV ibandronate (IIBN), oral ibandronate (OIBN), oral clodronate (CLO) or IV zoledronic Acid (ZA). The model adopts a third-party payer perspective and estimates the direct medical costs and QALY over the remaining lifetime of hypothetical cohorts of patients with breast cancer and bone metastases. In this analysis skeletal morbidity rates (SMR) was considered as drivers of cost effectiveness. The model included assumptions about costs of drug, cost of SRE, utility values for time with and without SREs and relief from bone pain, mortality, and compliance with therapy. Canadian costs and treatment patterns were used to populate the model.
Results: Over a patient lifetime, the discounted cumulative number of SRE was lower for ZA (3.44 per patient) compared to all other options; PA (4.06), CLO (4.56), IIBN (4.59), OIBN (4.72), and PL (5.62). Treatment with ZA resulted in a cost saving of $7,518 per patient vs. IIBN, $5,134 vs. OIBN, $2,589 vs. PL, $680 vs. PA, and $79 vs. CLO. Discounted QALY per patient was higher with ZA (0.817), followed by PA (0.810), IIBN (0.802), CLO (0.790), OIBN (0.788), and PL (0.765). Therefore, ZA is the dominant option being less expensive and more effective than all other agents.
Conclusion: Zoledronic acid appears to be the most cost-effective bisphosphonate and should be considered as the standard of care in Canadian breast cancer patients with bone metastases.

419 POSTER

The place of PET-18FDG in the diagnosis of breast cancer (BC) recurrence in the patients with isolated elevation of CA15–3 – single center experience

R. Jarcau, H. Larbre, A. Cuif, C. Pourny, R. Amir, J.C. Liehn. *Institute Of Oncology Jean Godinot, Reims Cedex, France*

Introduction: It is proved the performance of FDG-PET over conventional imaging in the diagnosis of the BC recurrence. There is no standard attitude