data suggest that a convenient oral ibandronate dose of 50 mg/day has a similar efficacy to intravenous zoledronic acid for suppressing tumor-induced bone resorption, but it is associated with a lower incidence of AEs following treatment. Effects on bone markers may indicate the comparable efficacy of the two bisphosphonates for the prevention of skeletal-related events. Thus, oral ibandronate may provide similar benefits to intravenous zoledronic acid for metastatic breast cancer patients, but with a superior tolerability profile.

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Biological functions of brain metastasis from breast cancer

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Secondary to the increased survival of breast cancer patients following chemotherapy, cerebral metastases have recently become a significant clinical problem, with an incidence of 30–40%.

The aim of this study was to characterize functional phenotypes that might enhance brain metastasis in human breast cancers. We used a computer program (PIANA) to build a protein interaction network for a collection of 19 proteins identified by MALDI-TOF. We were able to associate this network of proteins into 8 functional groups.

The METABRE gene analyses of 4 brain metastases made with U133plus2 Affymetrix chips has been used to assess differentially expressed genes in brain metastases compared with a pool of breast tumors, after normalization using the RMA (Robust Multichip Averaging) algorithm. From this analysis we obtained 5.235 candidate genes, 2.467 overexpressed (> 2 fold) and 2.768 underexpressed (< 2 fold). We matched these genes with the PIANA brain network.

As a result we found 179 proteins, 122 overexpressed and 57 underexpressed, in the brain metastasis network belonging to the following functions: 23 protein folding and chaperones; 9 ubiquitination; 36 signal transduction and receptors; 13 kinases; 4 immunological; 5 protein transport; 4 peptidases; 12 structural; 9 cell adhesion; 22 DNA binding, repair and transcription; 8 REDOX; 4 carbohydrate and 7 lipid metabolism. Ten of these proteins belong to the METABRE specific brain metastasis signature: ARFGAP, RNF25, EHMT2, TOP1, RNPC2, eIF-3, MCM4, GRP 94, FN14, and INHA. Some of these are being validated in tissue samples with specific antibodies.

These results provide evidence that the characteristic phenotype of brain metastasis includes specific cell-cell and cell-matrix adhesion, a cohort of stress-inducible proteins, REDOX and detoxification pathways, and lipid and glucose metabolism.

Study supported by Ministerio de Sanidad y Consumo FIS/PI041937 and by the EC MetaBre contract No. LSHC-CT-2004-506049.

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A multicenter phase II study of epirubicin with low-dose trastuzumab as a first line treatment in Her-2 overexpressing metastatic breast cancer: preliminary results

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Aims: To evaluate the activity and cardiac safety of the combination of epirubicin (E) with low-dose trastuzumab (LD-H) in patients with HER-2 overexpressing metatatic breast cancer.

Patients 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 (⩾12 objective responses/21 patients), the dose of H was mainatined to 1 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 ⩽10% of patients at an E dose of 720 mg/m^2 or in ⩽20% of patients 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 ⩽ 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 (C.I.95%: 5. 5–14.1) and the median overall survival was not reached.

Conclusions: These preliminary results show that the combination of E plus 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.

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Subjective assessment of breast cancer related symptoms, activity levels and quality of life of patients with metastatic breast cancer under treatment with Anastrozole

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Introduction: Third generation aromatase inhibitors have earned their place in first-line therapy for advanced breast cancer with proven superiority over tamoxifen. Particularly relevant in this setting are quality of life and activity levels of the patients from a patient perspective, based on objective response-parameters.

Material and Methods: Over a period of 12 months, a total of 466 patients with metastatic breast cancer either to one (n = 272) or multiple sites (n = 167) were questioned in 3 monthly intervals, and the responses were analysed, for the following:

1. Subjective breast cancer related symptoms based on a score from 1 (no symptoms) to 4 (severe symptoms).
2. Personal activity levels based on a score from 1 (full activity, no symptoms) to 5 (bedridden, unable to provide for oneself).
3. Quality of life based on a score of 1 (excellent) to 7 (very poor).

Results: The median age was 61.7 years (35–94). At the start of the 12-month period 31% of the patients was asymptomatic. After 12 months this percentage had increased to 41% and the degree of reported moderate to severe symptoms reduced in this timeframe from 41% to 28% of syptomatic patients with an average score reduction from 2.8 to 2.2. A worsening of symptoms during the therapy was seen in 151/466 (32.4%) of patients. In 73/466 (15.7%) this reduction was first reported after 3 months of therapy had been completed. The percentage of patients with restricted activity was lower after 12 months 46.2% compared to 57.2% at the start of therapy. The group who classified their quality of life as excellent increased over this time-period from 3.6% to 12.8%, reflected in an increase in average score from 3.0 to 3.7.

Conclusion: The aromatase inhibitor anastrozole is a highly effective palliative treatment for metastatic breast cancer demonstrated by a reduction in symptomatic disease and a corresponding increase in activity levels and quality of life in the majority of patients over a period of 12 months.

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Brain metastases in HER-2 positive metastatic breast cancer (MBC) patients

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Background: Several recent reports suggested relatively high risk of brain relapse in HER2-positive breast cancer patients. This phenomenon has been attributed to either an aggressive behavior of this tumor type and/or an increased survival following trastuzumab therapy without brain protection owing to insufficient penetration of this drug to CNS. In this study we