

had no further effect in increasing the sensitivity to oxidative stress. Taken together, these results suggest an important role for Prx II and Prx III in the protection of cells against oxidative stress in general and in the mechanism of lung metastasis in particular.

Future studies will explore the importance of the different cellular redox pathways in the metastatic process by further silencing (thioredoxin) or chemically blocking (catalase, glutathione system) various members of the redox system.

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421 **An electronic data registry for the evaluation of fulvestrant in clinical practice**

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Fulvestrant (Faslodex) is currently licensed for the treatment of postmenopausal women with advanced breast cancer following relapse or progression on antioestrogen therapy. However, it is unclear how this agent is being used in clinical practice. An electronic data registry was developed to provide insight into current fulvestrant usage and to collect clinical outcomes data. The electronic registry was designed by MedNet Solutions, which enabled participating centres to enter data via a secure Internet site. Data from 213 patients from 34 physician practice sites were submitted, of these 196 patients (92%) have now discontinued fulvestrant treatment and 17 patients (8%) are ongoing. Almost all patients (200/94%) had received prior endocrine therapy including tamoxifen, anastrozole, exemestane, letrozole, toremifene, or megestrol acetate. One-hundred-and-thirteen patients (53%) had prior exposure to tamoxifen, of these 51 (45%) had metastatic disease that had progressed on tamoxifen. A total of 1500 fulvestrant injections have been administered with patients receiving a mean of seven injections (range: 1-31). One-hundred-and-two patients (48%) gained clinical benefit (CB, complete response [CR, n=3], partial response [PR, n=52] or stable disease ≥ 24 weeks [n=47]) with fulvestrant treatment. In patients experiencing a CR or PR the median time to response was 2.0 months (range: 0.6-8.3 months) and the median duration of response was 4.7 months (range: 0.9-21.9 months). One hundred and fifty-eight patients (74%) have now progressed with a median time to progression of 4.6 months. Of the 196 patients who have completed fulvestrant treatment, 155 (79%) have received subsequent therapy, most commonly chemotherapy (55%). The electronic registry is a useful tool to monitor usage of fulvestrant and obtain outcomes data in clinical practice. These data support previous observations that fulvestrant lacks cross-resistance with other commonly used endocrine treatments and is a valuable new addition to the endocrine treatment sequence for patients with advanced breast cancer.

422 **Characterization of brain metastasis from human breast cancer in nude mice: longitudinal MR studies at 7 Tesla**

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The current incidence of brain metastases seems to be the paradoxical result of the effectiveness of drugs that do not cross the blood-brain barrier (BBB). The aim of this study was characterize in vivo functional phenotypes that might be correlated with enhanced resistance to therapy in brain metastasis. For this, we optimized a model of brain metastasis by internal carotid injection of brain metastatic cells (435-Br1) from a well known breast cancer cell line MDA-MB-435, from which we had previously identified 19 differentially expressed proteins. We obtained morphologic and metabolic magnetic resonance (MR) analyses at high-field (Bruker PharmaScan, 7.0 Tesla). Tumour growth in female BALB/c nude mice was characterized by T2, CE-T1 (Gd-DTPA, i.v. 0.2 mmol/kg) and diffusion weighted imaging ($b=100, 400, 800 \text{ s/mm}^2$), and also by single voxel 1H MRS (TE 35 and 136 ms). Metastases were detected in vivo at different progression stages by T2 and CE-MRI in 5 of 7 mice inoculated. ADC maps showed higher values for metastasis than for non-affected tissue: 0.89 ± 0.07 and $0.55 \pm 0.02 \text{ } (\times 10^{-3} \text{ mm}^2/\text{s})$, respectively, implying low tumour cellularity as confirmed by histology. MRS pattern changes indicate replacement of normal brain parenchyma by aggressive tumour cells (high Cho, low NAA). Tentative pattern recognition analysis of selected spectra, carried out in a Decision Support System (DSS) developed for human brain tumour spectra classification, INTERPRET SV (<http://azizu.uab.es/INTERPRET/>),

placed the spectral patterns in a clear progression towards malignancy, resembling human cases of healthy tissue being replaced by low grade glioma and finally evolving towards an aggressive pattern (GBM/metastasis). IHC analyses of tissues led us to the assessment of the specific protein expression in metastasis induced by brain microenvironment. In conclusion, we have characterized by MRI and 1H MRS a model of brain metastasis developing a possible non-invasive tool for brain metastasis staging and grading in animal models to use in experimental treatments.

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423 **Fulvestrant in postmenopausal women with metastatic breast cancer progressing on prior endocrine therapy – updated results from an expanded access programme**

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Background: Fulvestrant (Faslodex) is an oestrogen receptor (ER) antagonist with no agonist effects. Fulvestrant downregulates the ER, which leads to reduced cellular levels of progesterone receptor (PgR). This abstract reports the results of an expanded access programme in the Czech Republic (supported by AstraZeneca) in which postmenopausal women with metastatic breast cancer whose disease had progressed on prior endocrine therapy were treated with fulvestrant 250 mg.

Methods: Fulvestrant 250 mg was given as a single 5 mL intramuscular injection, once every 28 days until disease progression or other event necessitating withdrawal. Tumour response was assessed monthly using Union Internationale Contre le Cancer criteria. Time to progression (TTP) was defined from start of treatment until objective disease progression. Duration of response (DOR) was defined, for responding patients only, as the time from treatment initiation to disease progression.

Results: Between 8/2001 and 4/2005 a total of 64 patients (median age 66 years [range 39-92 years]) were treated in our centre. 87% of patients had ER-positive and/or PgR-positive disease. All had received prior endocrine treatment for advanced disease and 62% had received adjuvant endocrine treatment. Forty-one patients (64%) had also received prior chemotherapy. Thirty-two patients (50%) were receiving fulvestrant as their 3rd- or 4th-line endocrine treatment for advanced disease. Five patients (8%) had an objective response (1 CR and 4 PR). All responses were greater than 90 weeks in duration. Thirty four patients (53%) had stable disease (SD) ≥ 24 weeks giving an overall clinical benefit rate (CR + PR + SD ≥ 24 weeks) of 61%. The median TTP was 26 weeks. Fulvestrant 250 mg was well tolerated and no WHO grade III/IV toxicities were observed.

Conclusion: Fulvestrant 250 mg is an endocrine agent with demonstrable efficacy and a very favourable tolerability profile in patients with advanced breast cancer. The monthly injection schedule supports both close patient monitoring and good compliance. Fulvestrant offers clinicians a new option for the treatment of postmenopausal women with advanced breast cancer progressing on prior endocrine therapy.

424 **Every two-weeks docetaxel in the treatment of elderly patients with advanced breast cancer**

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Background: The study was conducted to investigate the efficacy and toxicity of bi-weekly docetaxel administration in elderly metastatic breast cancer patients.

Patients and Methods: Women aged ≥ 65 years with histologically confirmed metastatic breast cancer were eligible for enrolment. Patients could have received prior systemic adjuvant chemotherapy. Docetaxel was given as first-line (after adjuvant chemotherapy) in 10 patients and as second-line in 21 patients; 10 patients were pre-treated with anthracyclines regimens. Docetaxel was administered at 50 mg/m^2 as 1-hour intravenous infusion every 2 weeks. Docetaxel dose was reduced by 25% for grade 2 neurologic toxicity, febrile neutropenia, grade 3 thrombocytopenia or of any grade 2 non-hematologic toxicity. Patients were premedicated with dexamethasone 4 mg i.m. taken the night before, morning of, and evening after treatment. Patients continued to receive treatment until they developed either undue toxicity or until the time of disease progression.

Results: A total of 31 metastatic cancer women were entered into this study. The median age was 72 (range 65-78). ECOG performance status for all patients was 0-1. Most patients (21) had received prior chemotherapy, 10 patients had received first line anthracycline containing regimens. A total of 374 infusions were administered, 13.3 median, with a cumulative dose of $18,420 \text{ mg/m}^2$ (1083 mg/m^2 median). The projected