O-86. Trastuzumab and CerbB2 positive brain metastases – treatment synergy leading to longer survival?

Church DN, Braybrooke IP, Bahl A, Hopkins KI, Price GGA. *Bristol Haematology & Oncology Centre*

Trastuzumab (T) in combination with chemotherapy or as single agent is proven to extend survival in metastatic breast cancer (MBC) overexpressing c-erbB2. Studies have noted a higher than expected incidence of brain metastases (BM) in patients (pts) with MBC receiving T.

We have performed a retrospective review of pts with MBC receiving T in our institution between May 2002 and the present day.

12 of 54 (22%) of pts treated with T have developed BM. 2 pts with multiple BM and poor performance status (WHO>2) died before planned whole brain radiotherapy (WBRT) could be given. Those remaining have continued T (8 pts) or started T at time of diagnosis of BM (2 pts with brain as first site of metastasis) and have received WBRT plus further treatment with neurosurgery (1 pt), stereotactic radiosurgery (1 pt), and systemic chemotherapy (6 pts). Median survival for these pts is 12 months (range 3–36 months) with 7 pts alive at present. Notably, one woman with symptomatic progression of BM 6 months after WBRT showed partial response (PR) of BM to carboplatin chemotherapy maintained for 6 months and at progression a further PR to capecitabine. Another patient with multiple BM was treated with T and WBRT and is currently asymptomatic on maintenance T with no radiological evidence of BM 36 months after BM were diagnosed.

The favourable findings in our patients raise the possibility that continuation of T in women with BM may result in clinical improvements in survival. Although T is a large molecule that does not cross an intact blood-brain barrier (BBB) the disturbed BBB noted in BM may allow sufficient concentrations of T within BM to synergise with radiotherapy and chemotherapy, a phenomenon well demonstrated in pre-clinical work. Our findings require confirmation in prospective clinical trials.

O-87. Seeing through "chemo-fog" – myth or reality

Jenkins V, Shilling V et al. *University of Sussex*

The debate continues over the degree to which chemotherapy for the treatment of breast cancer affects cognition because previous studies have lacked pre treatment performance scores and used different analyses to calculate impairment. We report the cognitive performance on 93 women with breast cancer following treatment with standard chemotherapy compared to 43 healthy controls together with self report measures of quality of life, psychological well being and cognitive failure. At baseline patients and controls had similar cognitive functioning. There was an overall improvement in performance on four tasks (2 working memory, 1 processing speed and 1 executive function) however the patient group performed significantly worse than the control group on three tasks (AVLT supraspan $p = 0.045$; AVLT total score $p = 0.024$; (verbal memory) Stroop $p = 0.01$ (executive function). Using a statistical method that calculates change in individual performance (reliable change analysis) 12% of patients and 5% of controls were reliably impaired at the second assessment relative to baseline whereas 15% patients and 9% of controls reliably improved. The evidence suggests that only a small proportion of women experience objective measurable change in their concentration and memory following standard chemotherapy.

O-88. Effect of grape procyanidins on intracellular calcium levels in human breast cancer MCF 7 cells

Zhong JY, Zhang LH. *Nutrition Institute, Medical College of Qingdao University, Qingdao, PR China*

The effect of grape procyanidins (GPC) on intracellular calcium ($[Ca^{2+})]_i$) as well as cell proliferation and apoptotic levels was investigated in human breast cancer MCF 7 cell line. Cells were pre-treated with 0, 5, 50, 100 and 200 mg/L of GPC, and Fura 2AM, MTT assay and cell death detection ELISA were subsequently applied to detect $[Ca^{2+})]_i$, proliferation and apoptosis. GPC induced a significant concentration dependent increase in $[Ca^{2+})]_i$ levels: 3.2 folds with 50 mg/L, 7.6 folds with 100 mg/L and 10.3 folds with 200 mg/L of GPC compared with the cells without GPC treatment. GPC also showed to increase the release of calcium by endoplasmic reticulum. The proliferation of MCF 7 cells treated with GPC at the dose range of 50–200 mg/L was significantly inhibited by 21.4–56.2%. Furthermore, elevated apoptotic levels were observed with GPC treated cells. Apoptotic level was increased by GPC from 0.105± 0.003 (0 mg/L) to 0.537± 0.005 (50 mg/L), 0.717± 0.003 (100 mg/L) and 0.954± 0.006 (200 mg/L). All the increase was significant ($P < 0.01$). The massive increase in $[Ca^{2+})]_i$ and apoptosis as well as the reduction of cell proliferation suggest that grape procyanidins exert cytotoxic effect in MCF 7 cells. Clinically this implies that grape procyanidins intake might play a beneficial role in human breast cancer treatment.

O-89. Biochemical properties of breast cancer derived exosomes

Down SK, Berditchevski FB, Rea DW. *CRUK Institute of Cancer Studies, Birmingham*

Exosomes are vesicles secreted by tumour cells, which are enriched in tumour specific antigens, costimulatory and MHC class I molecules. They have been used to stimulate cytotoxic T cell responses against breast cancer cells *in vitro*, and have great potential in immunotherapy. A successful phase I clinical trial in melanoma has been completed. Tetraspanins are proteins expressed on exosomes which have important roles in cell signalling and adhesion. Both CD9 and CD82 expression have been shown to correlate with metastasis in breast cancer.

We isolated exosomes from established breast cancer cell lines and normal breast epithelial cells, and examined the expression of various tetraspanins under different culture conditions. Using SOS-PAGE and Western blotting we detected the presence on exosomes of MHC class I and tetraspanins CD9, CD63, CD81, CD82 and CD151. When cells were cultured with interferon gamma for 3 days, the expression of MHC class I increased markedly. In addition, novel tetramers of CD9 and CD151 were detected, and CD63 expression also increased. We