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Not threatening, though aggravating

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Background: About 80 women with pain in their breast participated in a test at the Jeroen Bosch Hospital at Den Bosch with GLA as medical treatment. The analysts are careful with the test results, but they assume that two out of three of the women who choose to co-operate on this test experienced good results. A more elaborated analysis is expected.

Not threatening, though aggravating: Pain in one or both breasts is a very important symptom at the patients who visit our breastclinic. The fear for breast cancer plays a part in it, however the chance on breast cancer at these patients is only about 0, 5%. Yet, a part of the women is interfered in such a way by this pain during practicing daily activities, they therefore visit a doctor.

Mastopathie is a repeatedly occurred complaint which can spontaneously appear and disappear and about 70% of the women once in their live trouble with. The complaint can early in the puberty appear and stays till an high age. Mastopathie can vary from a stressed feeling in the breast till an heavy pain which can affect the quality of live. The pain occurs both lateral as bilateral.

Recommendations: The diagnostic and treatment of mastopathie belong to the first line. But if there is uncertainty about the character of the pain or if the pain reacts inadequate on tranquilizing, conservative measures or painkilling, referring to the second line is an option. A solid anamnesis and physical examination, and if necessary an x-ray can tranquilize 85% of the patients in such a way that further treatment is not necessary. The other 15% of the patients are as such interfered by the pain that eventual medical treatment is useful.

At the Jeroen Bosch Hospital at 's-Hertogenbosch is now a test running with the use of GLA as treatment of a category mastopathic patients. Halfway 2008, a mastopathie-policlinic started at location Groot Zieken Gastenhuis. First the patients get a solid anamnesis (by the nurse practitioner and a surgeon) and an x-ray examination; the last one is necessary to exclude pathology and to diagnose and treat an eventual cyst, which can also cause pain complaints. After the diagnostic the women who would like a further treatment, start with omega 6 fatty acids in the shape of a GLA-preparations; 1x daily 90 mg GLA.

The past 6 months, 82 patients were treated in this way. At 70% of the patients were de pain complaints were certainly still present, but the VisualAnalogueScale-score decreased from 8 to 6. After 3 months, these women gave a Visual-Analogue-Scale score of 0−4. Two patients stopped taking the fatty acids because they experienced an increase of the complaints. As a result, this treatment appears to be a good adequate treatment for 2 out of 3 women who would like a further treatment.

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Five golden tips improve to anticipate on the breast cancer patient

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Background: Women with breast cancer go sometimes already 48 hours after the operation home. The women are satisfied about this short-stay. It is the expectation that in the close future this short-stay at many places will be introduced and further shortening to day treatment will find place. For this reason a workshop with as input golden tips (still) improve to anticipate on the breast cancer patient. An instrument for nurses to make well informed choices for the nursing during the admission on the patient care unit.

Method: On account of a workshop for nurses working with breast cancer patients and listening to the story of two patients from one's own experience, nurses become itself more aware what happened with themselves and the patients during admission in the hospital.

Results: Nurses of the departments 7 North, A0, A2 and A3 become conscious of what happens by thereself and the patient around breast cancer.

Discussion/Conclusion: The points of interest are:
1. conscious professional attitude
2. knowledge around breast cancer/procedure/treatment
3. individual assignment
4. multidisciplinary co-operation
5. uniformity

Recommendation: In the autumn of 2009 there will be draw up a plan to give credit for the points of interest given up by the nurses themselves.

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Survivor's point of view after breast cancer

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Background: Cancer diagnosis creates stressful situations for women. Successful coping alleviates stresses, improves patients' quality of life and improves acceptance of treatment outcomes.

Material and Methods: We designed a qualitative study to investigate the survivor's point of views about living after breast cancer treatments and also the main coping styles they used against cancer. Participants were 51 women who had breast cancer treatments and attended to breast cancer follow-up clinic in ICBC (Iranian Center for Breast Cancer), Tehran, Iran. Informed consents were obtained. All of the attendees had face to face in-depth guided interviews, with one open-ended questionnaire. The interviews were audiotape recorded, and then translated verbatim and major themes extracted. The interviews intended to motivate the participants to describe their life experiences.

Results: All of the attendees had completed surgery, chemotherapy and radiation treatments. Their age were 42−60 years, all of them were married. The time period between the diagnosis and their interviews was 4−7 years.

Major themes emerged were: Trust in God and spiritual beliefs as an essential and extra resource for all patients to help them to overcome their cancer problems. Family and specially husbands' supports were as highly potent factors for patients' coping with the cancer.

Conclusion: Patients had heavily relied on their prayers. This relation with God offered intercession for their healing and made them powerful to response to the cancer. It seems better that, Clinicians and healers encourage patients to use their mental powers to overcome (positive mental powers to win against) their cancer. Also, they may be promoting "trust in God and spirituality" and "positive attitude" in all processes of the patients' life.

Nurses may be in a unique position to promote between patients and their family (especially husbands) from initial diagnosis to the survivorship.

Wednesday, 24 March 2010 18:15–19:15

POSTER SESSION

Targeted treatment

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A multicentre audit of HER2 positive Early Breast Cancers and the reasons why patients do not receive trastuzumab therapy

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Background: Various trials have shown substantial benefits from adjuvant Trastuzumab (Herceptin®) therapy in HER2+ early breast cancer (EBC). Trastuzumab was licensed for adjuvant therapy in EBC in the United Kingdom in 2006. The objectives of this multicentre audit were to determine the incidence of HER2 + breast cancers, the number of HER2+ EBC women who received Trastuzumab and to ascertain the reasons why some HER 2+ patients did not receive Trastuzumab.

Methods: Data was collected for all invasive breast cancers diagnosed at six UK centres over an 18 month period from 2007 onwards. All HER2+ invasive breast cancers diagnosed by a combination of IHC and FISH were identified using each centre's breast cancer database. Case-notes and online records were checked for the HER2+ EBCs and reasons noted if they had not received Trastuzumab.

Results: Over the 18 month period, 3424 patients were diagnosed with invasive breast cancer at the 6 centres. There were 478 (14.0%) HER2+ cancers (range 10.3 to 18.5% across the 6 centres). 386 of these were EBCs.

238 (61.7%) HER2+ EBC patients received Trastuzumab therapy (range 56.7 to 63.9%).

Conclusions: The incidence of HER2+ breast cancers is 14% with majority of these (80%) being EBCs. Only 60% of the HER2+ EBC patients received Trastuzumab.

The most common reasons for not receiving Trastuzumab were node negative small tumours considered to be at low risk of recurrence and the patients' age. Recent studies have demonstrated that being HER2+ is a significant risk factor for relapse in patients previously perceived to be at low risk i.e. small node negative grade 1 or 2 tumours and no HER2+ patient should now be considered low risk [1]. Further trials are required to evaluate whether elderly HER2+ patients who are only eligible for Trastuzumab after adjuvant chemotherapy may derive benefit from Trastuzumab alone or in combination with endocrine therapy.

Table 1: Reasons for not receiving Trastuzumab (n = 148)

Reasons	Number of patients (%)
Tumour size <10 mm, node negative	53 (35.8)
Small node negative tumours (size 11−20 mm)	16 (10.8)
Age	27 (18.2)
Comorbidities	20 (13.5)
Patients refused therapy	19 (12.8)
Miscellaneous reasons	13 (8.8)

References

[1] Tovey SM, Brown S, Doughty JC, Mallon EA, Cooke TG, Edwards J. Poor survival outcomes in HER2-positive breast cancer patients with low-grade, node-negative tumours. Br J Cancer 2009 Mar 10; 100(5): 680–683.

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Transfection of the gene e and later application of cytotoxic drugs in the treatment of breast multicellular tumour solid cancer

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Background: The low efficiency of conventional therapies in achieving long-term survival of breast cancer patients calls for development of novel options. The potential use of combined gene therapy is under intensive study. One approach uses the expression of genes encoding cytotoxic proteins that affect cellular viability. The *E* gene from >X174 encodes for a membrane protein with a toxic domain which leads to a decrease in the rate of tumour cell growth. To improve the antitumoral effect of the doxorrubicin in breast cancer cell, we investigated a combined suicide gene therapy using this drug and *E* gene *in vitro*, using MCF-7 breast cancer multicellular tumour spheroids (MTS).

Materials and Methods: We cloned the gene E >X174 genome and tested the possibility of using it as an anticancer reagent in multicellular tumour spheroid of breast cancer (MTS). We investigated a suicide gene therapy using gene E in vitro using MCF-7 breast cancer cells forming MTS. In order to determine the effect of the combined therapy (gene therapy and citotoxics) transfected MCF-7 MTS were treated with gradient concentrations of the drug diluted in the culture medium: paclitaxel, docetaxel and doxorubicin. We studied the action mechanism of the combined therapy: study of apoptosis and cellular cycle, and the modulation of the volumes of the MTS of tumour cells.

Results: Our results showed that the use of doxorrubicin in MCF-7 breast cancer MTS transfected with E gene enhanced the chemotherapeutic effect of this drug. This inhibition was greater than that obtained using the gene therapy or chemotherapy alone.

Conclusions: The transfection of gene E in MCF-7 MTS is able to increase the chemotherapeutic effect of drugs and specially is able to enhance the anticancer effect of the doxorubicin in comparison to the growth inhibition obtained using the gene therapy or chemotherapy alone. These results indicate that this combined therapy may be of potential therapeutic value in breast cancer.

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Hsp90 inhibition with 17AAG can sensitize human breast cancer cells to taxol

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Background: Taxol (paclitaxel) is a potent cytotoxic and cytostatic drug which is used against breast cancer. Unfortunately, some drug-treated tumor cells survive being selected for adaptive mutations or involving alternative pathways that confer drug resistance. Because multiple heat shock protein 90 (Hsp90)-dependent pathways ensure tumor cell progression and survival, Hsp90 inhibitors, such as 17-N-allilamino-17-demethoxygeldanamycin (17AAG), may be synergistic with other anticancer drugs. Here, we examined effects of combining of 17AAG and taxol on human breast cancer cells.

Materials and Methods: Paclitaxel conjugated to a fluorescent label, rhodamine-123, and 17AAG were used as single agents or in combination (each at nanomolar concentrations) in the experiments with cultured breast cancer cells (MCF-7 line). The drug-induced cytotoxicity was assessed in TUNEL, annexin V-staining, and clonogenic or MTT-assays. The Akt and Raf-1 levels were analyzed by immunoblotting. The pumping-drug-out function of P-glycoprotein was evaluated on duration of retaining of paclitaxel-rhodamine-123 inside the drug-treated tumor cells which are gradually liberated from the label.

Results: Longer intracellular retaining of paclitaxel-rhodamine-123 nicely correlated with the increased percentage of apoptosis in MCF-7 cells treated with both the drugs. The same tendency was also found in clonogenicity and MTT-assay. Such enhanced cytotoxicity seems to be partly associated with the 17AAG-induced inhibition of the Hsp90-dependent pumping-drug-out function of membrane P-glycoprotein. As generally accepted biomarkers of the Hsp90 inhibition, we revealed the specific depletion of Akt and Raf-1 in the 17AAG-treated cells. In addition to the P-glycoprotein dysfunction, the down-regulation of Akt and/or Raf-1 can also contribute to the intensification of apoptosis conferred by the drug combination.

Conclusion: The synergism in cytotoxicity under combining of paclitaxel and 17AAG appears to be due to (i) overcoming the P-glycoprotein-mediated multidrug resistance and (ii) promoting the apoptotic scenario in the drug-treated tumor cells, while both these causes are a result of the functional inhibition of Hsp90. Co-administration of 17AAG and taxanes may therefore be effective in combinatorial schemes of chemotherapy of breast cancer.

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Novel gold speckled silica nanoparticle (GSS) as madiators of tumour imaging and photothermal ablation (University of Florida and Kurume University, Cancer Nanotechnology Study Group)

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Background: Our group has recently developed Gold Speckled Silica nanoparticles (GSS) as multimodal contrast agents for fluorescence, magnetic resonance and photoacoustic tomographic (PAT) imaging. The near infra red (NIR) optical absorption property of these particles makes them potentially useful for therapeutic applications such as for thermal ablation of tumors

Hypothesis: GSS nanoparticles are biocompatible and can be used for *in vivo* photothermal ablation.

Methods: Fluorescent (Fluorescein isothiocyanate doped)-GSS nanoparticles were synthesized using the water-in-oil microemulsion method. The average particle size was determined to be ~100 nm by Dynamic light scattering and Transmission Electron Microscopy. For *in vitro* experiments, human breast cancer cells (BT474) were incubated with pegylated and Fluorescent-GSS nanoparticles (PF-GSS). The tumor cell uptake was assessed using flow cytometry and fluorescence microscopy experiments. After GSS exposure, cell viability was assessed by propidium iodide exclusion. For *in vivo* experiments, BT474 cells were implanted subcutaneously in nu/nu mice and tumors were allowed to grow to 0.5 cm. PF-GSS (30 μL, 10g/mL) or saline (30 μL as control) were injected intratumorally in animal models. In vivo imaging was performed using PAT and ablation was achieved by exposure to near infrared red (NIR) laser (500mW, 10min). Tumor ablation was determined by histologic analysis with hematoxylin/eosin to assess the distribution and extent of tumor ablation, 24 hours following photothermal ablation.

Results: (i) In *in vitro* experiments dose related uptake of PF-GSS by BT474 cells (20μl, 25.4±7.4%; 40μl, 46.4±6.6%, p = 0.001) was observed. PF-GSS were non-toxic to cells in culture as evidenced by propidium iodide assays. (ii) In vitro, GSS (10 mg/mL) increased the temperature by nearly 15ºC, when exposed to NIR laser (785nm, 350mA) x 300 seconds vs. only 1ºC for plain water. (iii) Following intratumoral injection of PF-GSS, particles could be clearly imaged with PAT. (iv) Histological analysis showed significant photothermal tumor ablation in treated tumors after illumination with NIR light that was not seen in control treated tumors.

Conclusions: GSS are novel, biocompatible nanoparticles, which are able to generate heat in response to NIR laser stimulation. In addition, these nanoparticles can be imaged by multiple imaging tools such as fluorescence and PAT. Our experiments demonstrate that GSS can be used as mediators of image guided non-invasive cancer therapy by photothermal ablation.