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First experience with gosereline and ibandronate as medical prevention in premenopausal patients with increased familiary breast cancer risk: The GISS study

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Surgical ovarectomy can decrease the risk for the development of breast cancer in premenopausal BRCA mutation carriers to approx. 50% (Rebbeck, 1999). Does temporary medical suppression of ovarian function provide an alternative with a higher acceptance by the affected women? In this randomised phase II study 100 premenopausal participants (P) with a life time risk for breast cancer of > 25% are planned to receive either a medical prevention with Goserelin 3.6 mg/4 weeks and Ibandronate 2 mg/12 weeks for 2 years or only intensified breast cancer surveillance according to standard recommendations. Primary aims of the GISS study are acceptance and compliance of this kind of medical prevention. Approximately 10% of the invited women have agreed to the participation in the trial. Up to now 30 P (13 with treatment and 17 as a control) have been included in this trial in 8 active centres. One patients has withdrawn consent directly after randomisation. A known BRCA mutation is present in 4 P. In the other P the familiarly risk can be described as: 1st degree relative with known BRCA mutation (1), 1st degree relative with breast cancer < 35 years (4), 1st degree relative with bilateral breast cancer < 50 years (2), More than 2 relatives with breast cancer, one < 50 years (11), 1st degree relative with ovarian cancer < 40 years (3), 1st degree relative with breast cancer < 35 and > 2 relatives with breast cancer (2),1st degree relative with bilateral breast cancer and > 2 relatives with breast cancer (3). Two or 3 affected 1st degree relatives are present in 7 and 5 P, respectively. The median duration on treatment by now is 12.3 months. Reported side effects (grade 2-4) are headache (11), orthostatic dysfunction (5), hot flashes (4), pain (4), menstrual spotting (4), vaginal dryness (2), nausea (1), myalgia (1), insomnia (1), fatigue (1). Up to now only one P has discontinued treatment due to pain in relation to the application of Ibandronate. Acceptance to a medical prevention with Gosereline and Ibandronate is low, however compliance and side effects of this intervention appears to be favourable. Medical prevention may present an alternative to surgical ovarectomy, if efficacy can be proven to be equivalent.

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Pineal hormone melatonin as a modificator of a sensitivity of cancer cells to cisplatin

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Background: Cisplatin-based combination chemotherapy displays significant antitumor activity against cancers of the testis, ovary, head and neck, and also lung. Despite its success against testicular cancer, its effectiveness in the treatment of other cancers is more limited because of acquired or intrinsic resistance. We considered of interesting to study whether melatonin may or may not play a role an sensitivity of cancer cells to cisplatin.

Methods and materials: The oncostatic effects of melatonin have been studied both in vitro and in vivo. In vitro by using MCF-7 human breast cancer cell line (cis-DDP-sensitive and cis-DDP- resistant (4-fold) cells) as a model, and in vivo by using metastatic Lewis lung carcinoma (3LL) in mice C57Bl/6. Cell proliferation rates were detected after melatonin (Sigma, USA) and cisplatin (Ebewe, Austria) treatment upon short-term and long-term incubation. Quantification of hormone status of MCF-7/S or MCF-7/DDP4 cells was performed using EnVision system (Dako, Denmark).

Results: It was shown that upon long incubation (5th day) with melatonin in a concentration range 0,01-1nM, an inhibition of the growth of the resistant human cell line was registered. The growth of parental MCF-7/S cells was inhibited only at the highest dose of hormone (1nM). Moreover, the incubation MCF-7/S and MCF-7/DDP4 with melatonin simultaneously with cisplatin significantly increased the cytotoxical index, compared to cisplatin applied alone. The cytotoxic effect was more cleally indicated in MCF-7/DDP4 cells upon long-termed incubation. Moreover, melatonin administration changed the expression of progesteron and estrogen receptors, p53 or bcl-2 proteins and E-cadherin on MCF-7/S and MCF-7/DDP4. In in vivo condition melatonin enhanced the sensitivity of resistant 3LL cells to cisplatin.

Conclusion: The data suggests that melatonin could exerts its oncostatic action toward cisplatin-resistant tumor cells as well in vivo as in vitro. The results lends supports for a possible role of melatonin as a modificator of cancer cells sensitivity.

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The chemopreventive effect of garlic on tumorigenesis

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The cancer inhibitory effects of garlic has been claimed for years. In our labaoratory, we demonstrated that garlic possessed chemopreventive ability both in vivo and in vitro investigations, such as, garlic inhibited DMBA induced cheek pouch carcinoma in hamsters; and; garlic protected NIH3T3 cells from carcinogen transformation, etc. Therefore, in this study, we