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A PHASE II TRIAL OF GOSERELIN (ZOLADEX) IN RELAPSED EPITHELIAL OVARIAN CANCER

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26 patients, median age 57.5 years (range 38-90 years), with relapsed epithelial ovarian cancer were treated with the LHRH analogue, Goserelin (Zoladex), given as a long acting depot preparation subcutaneously. Patients had previously undergone debulking surgery and treatment with platinum based chemotherapy. 22 patients had prior multiple sequential systemic treatments for ovary cancer. The sites of relapse were: pelvis (13), abdomen (18), ascites (8), lung (3), liver (5) and supraclavicular nodes (2). A median of 2 cycles of treatment were given, range 1-11. There were 2 partial responses, each of 6 months duration, and 3 patients had stable disease (of 3, 6 and 11 months duration). Goserelin (Zoladex) has modest antitumour activity in chemotherapy pretreated patients with advanced ovarian cancer. In view of its lack of significant side effects this treatment should be further explored clinically and possibly earlier in the course of ovarian cancer in patients who could be identified as unlikely to respond to cytotoxic chemotherapy after relapse or progression with platinum based chemotherapy.

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SPECIFIC BINDING SITES FOR GONADOTROPIN RELASING HORMONE IN HUMAN ENDOMETRIAL CARCINOMATA

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Specific low affinity, high capacity binding sites for Gonadotropin Relasing hormone (GnRH) have been discovered in human breast and ovarian cancer. We checked if simular binding sites are present in human endometrial cancer. Plasma membranes were incubated with (^{125}I, D-Ala^{6}-des Gly ^{10}) GNRH-ethylamide in the presence or absence of unlabelled GnRH agonist or other peptides. GnRH-binding could be demonstrated in all twelve tumor samples tested. The analysis of the binding data was consistent with a single class of low affinity (K_a= 0.8-1.4 X 10^{8} M^{-1}) and high capacity (Bmax = 134-142 X 10^{-12} M/mg membrane protein) binding sites. GnRH itself had similar binding characteristics, while oxytocin, somatostatin and thyrotropin relasing hormone did not crossreact with the binding sites. Photoaffinity labelling of endometrial carcinoma membranes revealed the presence of a specific single molecular weight component of 62 KDa. If this GnRH-binding site in endometrial cancer is functionally relevant, it could be used for new therapeutical approaches.

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DIFFERENT GROWTH RESPONSES TO ESTRADIOL IN TWO HUMAN ENDOMETRIAL ADENOCARCINOMAS HETEROTRANSPLANTED INTO NUDE MICE

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The tumor growth phenotype and growth response to estradiol were investigated. In two separate experiments, using 20 animals each, two different, estrogen receptor (ER) positive and progesterone receptor (PgR) negative human endometrial adenocarcinomas growing in nude mice were transplanted. Ten tumor bearing oophorectomized animals were treated with Estradurin^{R} (17βpolyestradiol phosphate) i m indicating 250-300 pg/ml plasma estradiol value during experiment, whereas remaining 10 oophorectomized animals were treated with normal saline as control.
Both tumors grew in oophorectomized animals with unchanged growth pattern which suggests an ovarian (estradiol) independent growth of these tumors. The estradiol treatment of tumor bearing animals, however, resulted in inhibited growth in the one and stimulated growth in the other tumor.
Our results have shown that an ovarian (estradiol) independent but estradiol sensitive growth phenotype exists in human endometrial adenocarcinomas growing in nude mice. Growth response to estradiol, however, may be either inhibition or stimulation.

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Acute and Chronic administration of long-acting dopaminomimetic (LAR bromoscriptine) and somatostatin analogue (osteotride) in acromegaly

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Medical treatment of acromegaly involves the administration of dopaminomimetics i.e lisuride and bromocriptine or somatostatin analogues i.e octeotride or somatuline. In order to assess whether there is a differential sensitivity in the acute response we tested LAR bromocriptine 50 mg i.m or octeotride 25 µg s.c. Blood was collected prior to and for 12 hours after LAR and hourly for 4 hours after octeotride in 4 active acromegalics. LAR suppressed GH to a mean of 38% (range 18-66%) in 3 out of 4 whereas in the same patients octeotride suppressed to a mean at 75% (range 74-82%). In the fourth patient (who was normoprolactinemic) GH values suppressed by 83% to LAR and 90% to octeotride. Serial measurements of GH (4-24 daily) were made weakly or bi-weekly for a six month therapy with either agent. Chronic administration of LAR in the first 3 failed to maintain this suppression whereas octeotride maintained its effectiveness. In the 4th patient agent was equally effective.
This data suggest that the acute test with LAR or octeotride may predict chronic responsiveness and that octeotride seems to be more consistent and effective in the treatment of unselected patients with acromegaly.