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COMBINED TREATMENT MODALITY OF ESOPHAGEAL CANCER: RADIATION THERAPY (RT) WITH PHOTODYNAMIC THERAPY (PDT).

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Introduction: Surgery is still now the treatment of choice for esophageal cancer. However, this tumor, frequently, is been detected late. None of the available conventional treatment modalities may offer a long term survival.
Methods: Between 1982-1996 ,74 patients with esophageal cancer (all stages), have been treated with PDT and radiation therapy We applied 2 sessions of PDT in addition to radiation therapy (Linear Accelerator: 50 Gy + 10 Gy Boost).A second group of 75 patients was treated, between 1990 - 1996 only with radiation therapy (50 Gy + 10 Gy Boost).From this group, 41 patients received also chemotherapy(CT), 5 Fu +Mitomycin.
Results:In the first group (RT+PDT) the average survival time was: Ca. in situ 44 Mo., Stage I :25 Mo., Stage II: 29 Mo.,Recurrence: 20 Mo., Median: 37 Mo. In the second group (RT or RT CT) the average survival time was Stage I :) Mo., Stage II: 20 Mo., Stage III-IV: 8 Mo. We did not notice significant statistic different between RT+Ct and RT treatment alone.Therefore stage I and II patients might have a profit from RT+PDT versus RT or {RT+CT}.
Discussion: Because of staging differs between the groups,statistical comparison of the treatment modalities is not possible. Based on the literature, we can confirm that PDT combined with RT has shown to be a valid treatment, especially with low stage esophagus cancer, prolonging survival significantly.

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INTRAPERITONEAL THERAPY WITH INTERLEUKIN-2 (nIL-2) IN PATIENTS WITH OVARIAN CARCINOMA - PRE-CLINICAL AND CLINICAL RESULTS

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Despite a remarkable chemosensitivity in 75 % of patients with ovarian cancer 5 yr-survival rates range about only 35 %. Thus, we examined in an innovative orthotopic model with human ovarian carcinoma xenografts in athymic mice the antineoplastic effects of the cytokines IL-2, TNF-α, IFN-α, as single therapy or combined either with Taxol or Cisplatin. A total number of 362 animals were xenotransplanted and therapy was administered for 4 weeks. Within the monotherapy study groups IL-2 was the most effective cytokine. In this experimental series it was shown that combinations of different cytokines with chemotherapeuticals, which were not effective as single agents, were able to inhibit tumor growth, significantly. In a clinical phase I/II pilot study we administered 21 cycles of IL-2 i.p. via Tenckhoff catheter to 4 patients with ovarian cancer. No severe toxicity WHO grade III/IV was observed.
In conclusion, even high doses of nIL-2 given i.p. are very well tolerated and provide not at least by pharmacokinetic advantages a promising therapeutic approach to ovarian cancer.

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Interleukin 12: Generation of a cellular immune response against autologous single tumour cells of GIT-carcinoma

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Interleukin 12 is a potent inducer of IFN-γ secretion and immune cell proliferation / activity. It's antitumour effects are likely to be mediated by NK cells and preactivated T-cells, which have already been in contact with an existing tumour, but do not develop an effective immune response by itself. In vitro generation of this effective response against autologous single tumour cells was tried by short-term stimulation with IL-12.
Methods: From preoperative blood samples of 8 patients undergoing curative surgery for GIT carcinoma peripheral mononuklear cells were isolated by Ficoll-density-centrifugation and incubated (effectors): a) without stimu-lation (NK), b) with 100 I.U. IL-12/ml medium, and c) with 1000 I.U. IL-2/ml. From the resected carcinoma autologous single tumour cells were isolated by enzymatic dissociation. Using a fluorescence-cytotoxicity-assay, specific cytotoxic activity of effectors against following target cells was determined: a) autologous tumour cells, b) NK-sensible cells (K 562), c) allogeneic GIT tumour cells (RF 48/HT 29).
Results and Conclusions: The mean specific cytotoxic activity of PBL without stimulation (NK) against the three different targets was not significantly different. IL-12 always enhanced cellular activity. In contrast to moderate elevation against allogeneic targets, activity against autologous targets increased more than 3,1 fold ($p<0,05$), whereas generation of LAK cells by IL-2 only caused slight elevation. After the same IL-12 stimulation, specific activity against autologous targets was 2,3 / 2,8 fold higher than corresponding activity against K 562 / allogeneic GIT tumour cells ($p<0,05$). Significant stimulation by IL-2 was only seen against K562. These findings indicate IL-12 generation of a potential specific immune response by T8 lymphocytes according to thr operation profile of IL-12.
Clinical relevance of immunotherapy with IL-12 may implicate generation of a response against systemic dissemianted tumour cells associated with minimal residual tumour disease, especially as an adjuvant tool after operative tumour resection.

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SUCCESSFUL POSTSURGICAL IMMUNOTHERAPY OF PATIENTS WITH III-IV STAGES OF CANCER.

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We developed multi component cancer vaccine, that was shown efficient against metastases in animal models and in human patients. Here we will describe our clinical data. 27 patients with histological confirmed diagnosis and regional and/or distant metastasis (III-IV stages) received vaccine treatment after radical or subtotal surgery. No other type of therapy was applied to these patients. After radical surgery one year or more of survival and disappearance of all clinically detectable signs of disease was observed in 11 out of 12 cases (92%). Only 14 out of 56 (25%) patients survived without vaccine therapy. One year or more of survival without disease progression was observed in 4 out of 15 (27 %) patients after subradical surgery and vaccine treatment. Nobody survived in control group of 61 patients.

Our vaccine includes cellular and viral components. X - irradiated autological tumor cells, allogenic cells from 2-3 patients with the similar tumor histology and xenogeneic embryonic cells from distant species were mixed with symplast forming oncotropic virus. The mixture was injected into the patients intradermal once a week during 3-4 months.

Giant multinuclear cells that was formed intradermal as a result of the viral induced fusion of vaccine and host cells were highly immunogenic.

Immunotherapy was efficient for patients with most common and rare tumor localization.