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TREATMENT WITH r-INTERFERON ALFA-2b IN PATIENTS WITH RENAL CELL CANCER, AFTER SURGERY.

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Between January 1990 and December 1992, 23 renal cell cancer patients were evaluated.

All patients underwent abdominal approach surgery, with wide resection of the perirenal fat, early linc of the vascular pedicle and regional adenopathies removal.

Routine presurgical studies were performed to evaluate diagnosis and stages. All patients received no previous treatment: 4 with perirenal fat invasion and 3 with vascular pedicle invasion.

All of them were given a similar treatment schedule: Interferon Alfa-2 B SC, 10 MIU three times a week during 3 months with concomitant radiotherapy of the surgery lodge. Total dose: 4.000 rads.

Results: 19%. Four patients died before six months of treatment. Three of them showed vascular pedicle involvement and the remaining one showed perirenal fat invasion. Thirteen patients alive (58%); two with progression of the disease (distance metastasis). The remaining one showed no signs of progression of the disease.

Conclusions: The association between surgery, radiotherapy and Interferon Alfa-2b yields better results than the individual application of each.

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ELEVATED SERUM LEVELS OF CIRCULATING INTERCELLULAR ADHESION MOLECULE I IN PATIENTS WITH LIVER DISEASE TREATED WITH THYMOSTIMULIN.

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Sera of patients (pts) with liver cirrhosis (LC) or LC associated with hepatocellular carcinoma (HCC) or non Hodgkin's Lymphoma (NHL), were tested for circulating Intercellular Adhesion Molecule I (c-ICAM-I).

The detection of c-ICAM-I was carried out with a sandwich assay by using mouse mAb CL 207 and VF 275.16, provided by dr. S. Ferrone (New York Medical College, Valhalla, NY).

Seven pts were affected by LC, 9 pts by HCC+LC, 6 pts by NHL, and 10 pts by NHL+LC. One pt with LC, and 8 pts with HCC+LC were treated with Thymostimulin.

We found high serum levels (higher than mean control increased by 2 SD) of c-ICAM-I only in pts treated with Thymostimulin; while pts with LC or HCC+LC, not treated with Thymostimulin, displayed low serum levels of c-ICAM-I.

Therefore, we suggest that Thymostimulin treatment induces c-ICAM-I, which play a major role in a variety of cell mediated immunoreponse. Furthermore, considered the success reached in our patients with Thymostimulin treatment, we infer that c-ICAM-I can be a useful marker to prove the efficacy of the therapeutic regimen.

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The prognostic significance of cytotoxic capability in colorectal cancer patients treated with monoclonal antibodies.

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There are several evidences that the immune system might play a role in the pathogenesis of malignant diseases. In this study 44 patients with metastatic colorectal carcinoma paired with healthy controls were analysed for cytotoxic capability before start of immunotherapy with the mouse monoclonal antibody 17-1A (Mab17-1A). Peripheral blood mononuclear cells (PBMC) were used together with Mab17-1A in antibody dependent cellular cytotoxicity (ADCC) or alone in 18h- and 4h-assay against S948 colorectal carcinoma cells. PBMC were also used against K562 and Daudi. Patients showed an increased cytotoxicity against S948 (ADCC, 18h- and 4h-assay) but not against K562 or Daudi compared to controls. Patients with a cytotoxicity above the median value had a significantly longer survival compared to those below the median. This was true for ADCC, 18h-assay without Mab and K562 but not for the 4h-assay without Mab. If these four tests were combined the significance was enhanced ($p=0.000053$). The good responding patients had a median survival of more than 80 weeks compared to 38 weeks for those with a poor reactivity. There was no difference between the two groups in regard to age, sex, Duke's stage at surgery, tumor differentiation, number and size of metastases and levels of serum tumor markers. The responding patients had however a longer median time from primary surgery to development of metastases (14 vs 4.5 months, $p=0.004$). These results may indicate an influence of the immune system on the prognosis in this malignant disease. Maybe, the cytotoxic capability of the patients should be taken into consideration when including patients on immunotherapy protocols.

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TREATMENT OF NON-RESECTABLE CARCINOID LIVER METASTASIS WITH INTERFERONE ALPHA 2B

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Introduction: Human carcinoid tumors are known as only moderate chemotherapysensitive. On the other hand encouraging results after subcutaneous Interferone treatment has been published. Since 1988 we have treated 21 patients with liver metastasis by interferone alpha 2b.

Patients: Liver metastasis of 8 patients with carcinoid of the small bowel, of 6 pats. with bronchogenic carcinoid, of 2 pats with appendix carcinoid, in 1 pat of the colon, of 2 pats of the pancreatic tail and of 2 patients with unknown primary tumor could be detected; 6 patients had carcinoid syndrome with flush and/or diarrhea.

Schedule: 5 MIO I.U. Interferone alpha 2b were applied three times every week (Mo,Wed,Fri) subcutaneously.

In cases of progress we have combined Interferone with Fotemustine.

Toxicity: leukopenia WHO III in 1 pat, WHO II in 7 pats, thrombopenia WHO I in 2 pats, anemia: WHO I in 3 pats, inappetence with weight loss >CTC I in 5 pats.

Response: 1 (5%) CR, 2 PR (9%), 14 (67%) SD, 4 (19%) PD; 4/6 patients became an improvement of her carcinoid syndrome.

Conclusion: Interferone is an efficient agents in treatment of metastatic carcinoid disease with only moderate toxicity.

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THYMOSTIMULIN IS EFFECTIVE TREATMENT IN HEPATOCELLULAR CARCINOMA ASSOCIATED WITH LIVER CIRRHOSIS.

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Effective treatment for Hepatocellular carcinoma (HCC) associated with Liver Cirrhosis (LC) is not known. We obtained complete remission (CR) in 3 nonsurgical pts (2 males and 1 female) with HCC+LC by treated with Thymostimulin at the dose of 70 mg/die, 5 times a week. One of 3 pts was considered in progression of disease (PD) after alcoholisation, at the start of Thymostimulin treatment; the other 2 had not received any therapy. Patient characteristics are reported in the following table.

#	Sex	Age	HCC size (cm)	AFP (U/L)	Hepatitis Viruses Markers		Alcohol Abuse
					B	C	
1	M	63	6	920	-	+	+
2	M	63	8	6800	-	+	+
3	F	70	4	800	-	+	-

Patients achieved CR after 18, 3, and 6 months of treatment, respectively, and they are actually considered in CR, with overall survival of 53, 20 and 9 months, respectively. At date, these pts are still treated with Thymostimulin and treatment duration is 53, 20, and 7 months, respectively. On the basis of CR and long survival obtained, Thymostimulin could be an effective treatment in the cure of HCC associated with LC.

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IMMUNOMODULATORY EFFECT OF ROFERON IN PATIENTS WITH DISSEMINATED MELANOMA

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The proliferative response of human peripheral lymphocytes to T-cell mitogen phytohemagglutinin P (PHA) and the level of T-cells were analysed in patients with disseminated melanoma, treated with Roferon (Recombinant Leucocyte A Interferon). Roferon was administered subcutaneously at three millions units each weeks. The patients had previously been treated by surgery and chemotherapy with Dacarbazine, however no systemic anticancer treatment had been given within 8 weeks of commencing this study. An increase in PHA-responsiveness and T-cells was observed after Roferon treatment. Although in all patients an objective tumor regression was not found after Roferon treatment, subcutaneously administered Roferon induced immunological changes, and suggests that, subcutaneously given Roferon increased proliferative activity of lymphocytes and level of T-cells of this patients.