Diagnosis, Treatment and Prognostic Factors in Colorectal Cancer

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INTERFERON AND 5-FU IN ADVANCED COLORECTAL CANCER

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Treatment of advanced colorectal cancers remain unrewarding due to poor results. A randomised trial was carried out where in patients received either 5-FU, mitomycin C and doxorubicin (FAM) or interferon (rh IFN alpha2b) and 5-FU. Mid term analysis showed severe toxicity in FAM arm which was terminated. Of the 50 patients treated with interferon 3M.U subcutaneously on alternate days for 12 weeks and 5-FU 500 mg/sg mtr infusion for 5 days repeated every 21 days for 3 cycles, 44 evaluble patients showed the following results: complete response in 3(6.8%), partial response in 18 (40.9%), no change in 4 (9.1%) and progressive disease in 19 (43.2%). Toxicity observed were manageable. Mean duration of response was 3 months (range 0-7 months). This study shows an encouraging trend of improved response in the management.

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COMPARISON AMONG SERIC, IMMUNOHISTOCHEMICAL AND RADIO IMMUNO GUIDED SURGERY (RIGS) DETECTION OF CEA AND B 72.3 IN COLORECTAL CARCINOMAS

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Sixteen patients with primary and/or recurrent colo-rectal cancer underwent RIGS.Eight patients were injected with MAb B 72.3-1251 (Surgimab R3, Sorin Biomedica, Saluggia Italy) and eight with FAb antiCEA-1251 (Surgimab R2 Sorin). The former underwent surgery after 20-25 days, the latter after 8-10 days.
Radioactivity was measured by means of a gamma-detector probe Neoprobe 1000 (Columbus, Ohio) during surgery, and ex vivo on cancer and on suspected sites. Gamma emission values 1,5 fold higher than surrounding normal tissue were taken as positive. By RIA method, seric CEA levels were measured, while CEA expression was detected on formalin-fixed, paraffin-embedded samples, and B 72.3 on fresh tissue by immunohistochemical method. By statistical analysis, a linear correlation links RIGS and tissutal (CEA and B 72.3) data; on the contrary, seric CEA levels are not related to both tissutal and RIGS values.
Our preliminary results outline RIGS accurancy in the identification of neoplastic colo-rectal foci.

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CLINIC, MORPHOLOGIC AND BIOLOGIC CHARACTERIZATION OF 69 CONSECUTIVE CASES OF LARGE-BOWEL CARCINOMAS.

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69 patients (36 males, 33 females, median age 64 yrs) were admitted to the Department of Surgery of the University of Modena because of a diagnosis of large bowel adenocarcinoma (20 right colon, 40 left colon, 9 rectum). Before surgical treatment, serum levels of CEA and Ca19.9 were assessed. All patients underwent curative or palliative large bowel resection. Each tumour was staged according to the TNM System and grouped into four main categories. Cell proliferative activity was assessed by the immunohystochemical detection of Ki-67 nuclear antigen and by 5BrdU in vitro labeling index on fresh-frozen tissue. K-ras gene mutations were investigated by multiplex-ASPCR. Routinely fixed and paraffin embedded tumour specimens were examined to determine some morphologic parameters such as grading, pattern of growth, tubular configuration, lymphocitic infiltration, amount of eosinophils and fibrosis, and to assess the mean nuclear AgNOR number. Statistical analysis of results was carried out comparing all the studied parameters in contingency tables. Significant relationships were found between tumour stage and grade ($p<0,05$), Ki-67 value ($p<0,05$), and AgNOR number ($p<0,05$) to show that more advanced is the disease, higher are the Ki-67 and AgNOR values. Our results appear to suggest a possible relationship between the stage and some biologic features of the disease. However the value of these parameters as prognostic factors has to be verified in a successive survival study.

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AZIDOTHYMIDINE (AZT), 5-FLUOROURACIL (5-FU) AND L-FOLINIC ACID (FA): A PILOT STUDY IN METASTATIC COLORECTAL CANCER (MCRC).

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In preclinical studies we have demonstrated that 5-FU increases the incorporation of AZT in DNA of tumor cells and enhances its antitumor activity. We have initiated a pilot study in MCRC patients (pts) to determine the maximum tolerable dose (MTD) of AZT administered weekly in combination with 5-FU and L-FA and the antitumor activity of this combination. So far 28 chemotherapy naive MCRC pts entered the study. Therapy consisted of weekly 5-FU 500 mg/sqm i.v. bolus in the middle of a 2 hour infusion of L-FA 250 mg/sqm and AZT given as a 90' i.v. infusion starting 60' after 5-FU at the initial dose of 0.5 g/sqm. AZT dose was escalated of 0.5-1g/sqm in subsequent triplettes of pts if dose limiting toxicity had not occurred. So far the maximum dose of AZT administered has been 7g/sqm, a Cmax of 618 μM and an AUC of 186,400 μM/min have been reached and MTD has not yet been reached. Toxicities included mostly diarrhea (WHO grade [G] 1-2: 50%, G3: 14.3%), stomatitis (G1-2: 50%, G3: 3.6%) and dermatitis (G1-2: 50%, G3: 3.6%). Among 27 evaluable pts 4 complete responses (15%), 7 partial responses (26%) (response rate 41%; 95% confidential limit interval: 22-61%), 2 minor responses (7%), 9 stable disease and 4 progressions have been observed. The study is in progress. (Partially supported by A.I.R.C.)