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The peculiarity HLA-allels and HLA-lymphocyte phenotypes in the patients of Uzbek population suffering from colorectal cancer

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Introduction: The purpose of our study was the determination of peculiarity HLA-allels and HLA-lymphocyte phenotypes in the patients (pts) of Uzbek population (Uz.p) suffering from colorectal cancer (CC).

Methods: 77 pts with CC were studied. The HLA-typing class I was performed by routine lymphotoxic test with complement. The monospecific anti HLA-globulins were used.

Results: Study of distribution of HLA class I revealed reliable increased frequencies of HLA A28; B27; B8; B40 allels (p 0.05). Also were defined high level of predominance the unprofitable HLA-lymphocyte phenotypes, which was characteristic for many pts 96.1%. Three basic types of unprofitable HLA limphocyte phenotypes has been defined: I – total absence one or two HLA locuses 32.45%; II – absence some HLA-A; -B; -C allels 15.5; III-total absence of HLA locus and loose one of allels from other locuses. Only 3 pts had "full house" HLA-phenotypes 3.9%.

Concusion: The people with A28; B27; B8; B40 HLA allels are group of risk to the CC in Uz.p. The loss of capability for expression HLA-molecules in the immunocompetent cells may be also one of primary pathogenetic parts in the development of cancer diseases.

256 PUBLICATION

Oxaliplatin (L-OHP) in combination with leucovorin and bolus-continuous infusion 5fluorouracil (LV5FU2) in advanced colorectal cancer (ACC) pretreated with 5fu

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L-OHP is active against ACC both in 1st and 2nd line; in 1st line the combination with LV5FU2 demonstrated an increased activity in comparison to LV5FU2 alone (De Gramont, ASCO 1998). We performed a phase II trial in order to evaluate the activity of L-OHP + LV5FU2 in patients (pts) pretreated with 5FU.

From 4/96 to 3/99, 55 pts (34 male, 21 female; mean age 59.5 years; PS 0:22, 1:21, 2+ 3:12; liver mts: 38) with ACC progressing after 5FU-based chemotherapy entered this trial: in 24, 1st line treatment was bolus 5FU (modulated by LV or MTX or IFN) and in 31, infusional 5FU (LV5FU2 in 21, other regimens in 10). In 23 pts a 2nd or 3rd line therapy had been administered before entering the study. The treatment schedule was: L-OHP 85 mg/sqm every 2 weeks + 2 h 1-LV 100 mg/sqm and 5FU 400 mg/sqm bolus followed by 600 mg/sqm in 22 h infusion on day 1 and 2 every 2 weeks. In the 41 pts up to now evaluable (14 are early) we observed: 0 CR, 13 PR, 14 NC (with a tumor growth control in 66%) and 14 PD. The median time to progression was 5+ months and overall survival 7 months. Side effects were: peripheric neuropathy (grade 1–2: 25%, grade 3–4: 3.6%) and moderate myelotoxicity, mucositis and diarrhoea.

This treatment is active in 5FU pretreated pts and should be evaluated in comparison to CPT-11 ± continuous infusion 5FU.

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Oxaliplatin, 5-FU and folinic acid (OFFA) as II-line chemotherapy in advanced colorectal cancer

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Introduction: We report our experience with OFFA as II line chemotherapy in advanced colorectal cancer.

Methods: 26 consecutive pre-treated patients with advanced colorectal cancer were treated with oxaliplatin 130 mg/m^2 day 1°, 5-FU 375 mg/m^2 day 1°–>5°, folinic acid 20 mg/m^2 day 1°–>5°, every 28 days. All patients presented a progression of disease after I-line 5-FU-based chemotherapy, and an evaluable disease. Every two courses of chemotherapy, a restaging of disease was performed, and the treatment was discontinued for progression of disease or toxicity.

Results: Till today, 97 courses of chemotherapy have been performed in the 26 enrolled patients, with a median courses/patient ratio of 4 (range 1–8). All patients are evaluable for toxiciy, and 22 ones for response. We observed 1 partial response (3.8%), 9 stabilizations of disease (34.6%) and 12 progressions of disease (46.2%) with a time to progression of 71 days. Till today 12 patients are dead, with a time to survival approximatively of 10 months. No grade III–IV hematologic toxicity was observed, grade III diarrea and grade III mucositis were observed respectively in 2 (7.4%) and 1 (3.8%) patients, with no other grade III non-hematologic toxicities. Grade II and grade I neurologic toxicity were observed respectively in 8 (30.8%) and 9 (34.6%) patients.

Conclusions: OFFA represents an effective and well tolerated option when a progression of disease after 5-FU-based regimens occurs: our data could also suggest the use of OFFA as I-line chemotherapy besides as II-line one for advanced colorectal cancer. Supported by Istituto Oncologico Romagnolo IOR.

258 PUBLICATION

'Tomudex' (raltitrexed) has a manageable toxicity profile in elderly patients with metastatic colorectal cancer

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Introduction: 'Tomudex' is an effective alternative to 5FU as monotherapy in the treatment of adult patients with advanced colorectal cancer. A multicentre Phase II study was therefore conducted principally to assess whether the safety profile of 'Tomudex' extends to elderly patients in this setting.

Methods: Elderly patients aged >/=70 yrs with previously untreated or adjuvant treated advanced colorectal cancer were eligible for inclusion. 'Tomudex' 3 mg/m[2]/day was given by 15-min iv infusion every 3 weeks until disease progression or significant toxicity. Tolerability was principally assessed by monitoring the frequency of serious (WHO grade III/IV) adverse events.

Results: 51 patients (34 male, 17 female) with a median age of 75 yrs (range 70–89 yrs), and a WHO performance status of 0 (24 pts), 1 (20 pts), or 2 (7 pts) were included. 35 pts with colon cancer and 16 with rectal cancer had metastases at 1 (40 pts) or 2 (11 pts) sites located in the liver (33 pts), lung (10 pts), peritoneum (9 pts), bone (3 pts) or at other sites (7 pts). 14 pts had previously received adjuvant chemotherapy. 205 cycles (median 4, range 1–13) giving a median relative dose intensity of 95% (range 44–103%) have been delivered. Grade III–IV toxicities were seen in 24 pts (47%). Grade III/IV anaemia was seen in a total of 9 treatment cycles (6 pts, 12%), neutropenia in 2 cycles (2 pts, 4%), and thrombocytopenia in 1 cycle (1 pt required platelet transfusion, 2%). Other grade III/IV toxicites were: nausea/vomiting, 9 cycles (7 pts, 14%); diarrhoea, 6 cycles (5 pts, 10%); infectious disease, 6 cycles (5 pts, 10%); asymptomatic increase in transaminase activity, 13 cycles (12 pts, 24%). 10 pts (20%) experienced severe asthenia (12 cycles). There have been no toxic deaths. Among 35 pts evaluable for efficacy there have been 1 confirmed complete response and 8 partial responses (RR 26%). 14 pts (40%) experienced stable disease.

Conclusions: These preliminary results suggest that 'Tomudex' has a manageable toxicity profile in elderly patients with untreated metastatic colorectal cancer.

'Tomudex' is a trade mark, the property of Zeneca Ltd.

259 PUBLICATION

Preoperative radiotherapy for advanced lower rectal cancer-combination of external and high-dose-rate intraluminal radiotherapy

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Purpose: To evaluate the therapeutic results of preoperative irradiation using a combination of external irradiation and high-dose-rate intraluminal irradiation using 60Co (RALS) aimed at enhancing postoperative local control of advanced lower rectal cancer.

Methods: The subjects comprised 38 patients (31 men and 7 women) in whom "∫T3 lower rectal cancer was suspected and who underwent preoperative irradiation (RT group). A control group (N-RT group) consisted of 19 patients subjected to operation alone in whom postoperative histolog-