Sto 13**IS FAM AN EFFECTIVE DRUG REGIMEN IN THE ADJUVANT TREATMENT OF GASTRIC CANCER?**

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In advanced gastrointestinal cancer a combination chemotherapy of 5-Fluorouracil, Adriamycin and Mitomycin C (= FAM) proved to be a highly effective drug regimen with a more than 50% objective response rate (J. McDonald, P. Schein, Proceedings ASCO 17: Abstract C-111, 1976). As a consequence the efficacy of this treatment in an adjuvant setting of potentially curative resected cardiac and gastric cancers was investigated. From October 1981 through July 1984, the International Cooperative Cancer Group (= ICCG) entered 330 patients into a prospective randomized trial. The group consists of members from 22 hospitals in Europe and the USA. The patients who underwent an operative resection for carcinoma of the cardia or stomach were randomly assigned to either no further treatment or six 8-weekly courses of FAM according to the following schedule:

5-FU 600mg/m² days 1,8,29,36

Adriamycin 30mg/m² days 1 and 29

Mitomycin C 10mg/m² day 1.

The treatment was tolerated rather well by the patients. Stratification was performed according to localization and extent of tumor as well as lymphnode involvement. Altogether 28 patients are ineligible for analysis. The latest results regarding toxicity, recurrence rate and mortality are presented. Furthermore the results are analyzed with regard to tumor localization, histology, tumor stage and operative modalities. At present the group under adjuvant chemotherapy seems to have a small survival benefit. Special emphasis will be given to the question whether certain subgroups profit significantly from adjuvant FAM therapy.

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Sto 14**POLYCHEMOTHERAPY WITH METHOTREXATE IN MEDIUM DOSE RANGE, 5-FLUOROURACIL AND ADRIAMYCIN IN ADVANCED GASTRIC CARCINOMA**

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20 patients suffering from advanced gastric carcinoma were treated with a 3 drug combination chemotherapy containing Methotrexate (MTX) 300 mg/m² 5-Fluorouracil (5-FU) 900 mg/m² and Adriamycin (ADM) 40 mg/m² day 1. MTX (150 mg/m²) was given iv followed by a 4 hour continuous infusion of 150 mg/m² MTX. 5-FU was injected iv 7 hours after starting the MTX infusion. ADM was injected by iv bolus before or after MTX. To avoid toxicity due to MTX patients received 500 to 1000 ml of sodium chloride 0.9% or glucose 5% before and 3000 ml after application of MTX as well as sodium bicarbonate for alkalization. Leucovorine rescue was started 24 hours after MTX injection consisting of 22,5 mg Leucovorine x 8 given po or im at 6 hour intervals. Each course was repeated every 21 days. So far 20 patients entered the study. Age ranged from 32 to 66 years. 3 patients had received prior chemotherapy with different drug combinations. 10 patients had undergone surgical treatment. Karnofsky performance scores ranged between 60 and 100% prior to chemotherapy. In all patients the progress of the disease had been well documented. Total number of courses applied was 82 with a mean of 4.1 courses/patient (range 1 to 8). 10 patients responded with a measurable reduction of tumor size (response rate 50%). So far mean duration of remission was 4.9 months (range 1+ to 8+). It is emphasized that all responding patients showed a fast improvement in their overall clinical performance as there is reduction of pain gain of weight and improvement of Karnofsky index. 2 patients showed stable disease for 1.5 and 4 months. 8 patients did not respond to chemotherapy. Mean survival of 10 patients responding to chemotherapy is 7.8+ months (range 1+ to 13.5) with 4 patients still alive. Mean survival time of nonresponders was 3.6 months (range 1.2 to 7). Chemotherapy was well tolerated. Alopecia was seen in all patients. Minor side effects included nausea and fatigue. 6 patients suffered from stomatitis after each course. Mild transient leukopenia occurred in 3 patients, no septic complication was seen. Although remission incidence is not as frequent as in high dose MTX/5-FU + ADM regimens (Dtsch.med.Wschr.107,1708,1982), our preliminary data suggest that the combination chemotherapy with MTX in medium dose range, 5-FU and ADM is effective as well in advanced gastric carcinoma.

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Sto 15**PROGNOSTIC FACTORS IN ADVANCED GASTRIC CANCER PATIENTS RECEIVING CYTOTOXIC CHEMOTHERAPY**

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In this retrospective study tumor- and patient-related characteristics were correlated with survival and response in patients with advanced gastric cancer receiving cytostatic treatment. The following data of 147 patients, treated in 3 multicenter chemotherapy studies, were analyzed: age, sex, performance status, weight, type and success of operation, disease free interval, dosage and response of chemotherapy, histology, localisation of tumor and metastases, hemogram and serum parameters.

Survival was significantly prolonged in older patients, in patients with normal performance status, with primary curative resection, with lymphnode metastases, without liver or pulmonary metastases and in patients with initial normal white blood count (WBC) and initial normal levels of the following serum parameters: GOT, AP, bilirubin, urea and creatinine. Performance status, type of operation, levels of alkaline phosphatase, urea and WBC were found to be the most significant prognostic factors by using the multivariate Cox regression model.

Response rates were higher in patients with normal performance status, with curative resection, with diffuse type of Lauren classification, with peritoneal carcinosis and with normal levels of WBC, GOT and AP.

In a group of 118 patients response was more frequent in the diffuse type of Lauren with 27 % (16/59) vs. 14 % (8/59) in the intestinal type. The intestinal type was dominating in older patients, men and patients with liver metastases. In patients with two or more metastatic sites the diffuse type was seen more frequently.

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Sto 16**5-FLUOROURACIL, 4-EPIDOXORUBICIN, AND MITOMYCIN C (FEM) FOR ADVANCED GASTRIC CARCINOMA. A PHASE II TRIAL.**

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To assess the efficacy of 4-epi we conducted a phase II trial using a modified FAM combination with 4-epi instead of adriamycin. Patients received 5-fluorouracil 600 mg/m² day 1,8,29,36, 4-epi 45 mg/m² day 1 and 29, and mitomycin C 10 mg/m² day 1 i.v. Therapy was repeated after 8 weeks. Evaluation of tumor response was performed before the second cycle.

38 patients, 13 women and 25 men, with a median age of 59 years entered the study. In the 26 patients with measurable tumor 5 died within the first chemotherapeutic cycle (early death), 1 still could not be evaluated for response. Out of the remaining 20 patients we observed 0 CR, 6 PR, 9 SD and 5 P suggesting a preliminary response rate of 6/20 (30%). The median survival of 31 patients was 5.3 months, of the PR 9.3 months, and P 4.7 months, respectively.

FEM was well tolerated with moderate haematological toxicity and low grade alopecia. It does not show higher activity than FAM, but a dose escalation seems to be possible in future trial.

Chemotherapiegruppe gastrointestinaler Tumoren (CGT).