Methods: One hundred and three patients entered into the study. The experimental group received preoperative radiation therapy (n = 49), the control group-surgery alone (n = 54).

Results: Similar overall survival was observed in patients of the experimental and the control groups: median survival was 40 and 48 months, 3 year survival rate (YSR) 54 ± 7% and 54 ± 8%, 5 YSR 46 ± 8% and 44 ± 7%, 10 YSR 41 ± 8% and 31 ± 7% respectively. When various subgroups of patients were analyzed the results showed significant difference. The most impressive advantage of the combined treatment modality was seen when N positive cases were compared: median survival was 37 and 17 months, 3 YSR 50 ± 11% and 35 ± 10%, 5 YSR 45 ± 11% and 10 ± 6%, 10 YSR 28 ± 8% and 10 ± 6% respectively.

Conclusion: Adjuvant radiation therapy can improve surgical results in selected groups of patients with resectable gastric cancer.

543 PUBLICATION

The influence of trypsin, chymotrypsin and papain on the growth of human pancreatic adenocarcinoma transplanted to *nu/nu* mice

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Purpose: The aim of the study as presented was to investigate the influence of protease mixture in a model of transplanted human pancreatic carcinoma based on our previous results in mice syngenic tumor models.

Material and Methods: After the 2 weeks of postransplant latency, total of 18 *nu/nu* mice (CD-1 prone) bearing subcutaneously the human adenocarcinoma were as random divided into two equal groups. The 1st one (enzyme group) was administered with trypsin, chymotrypsin and papain solution rectally. The 2nd one (control group), was administered with saline by the same way. The tumour growth in both groups was measured daily for following 30 days and the tumor mass was calculated from their extents.

Results: Along the presented study, protease mixture retards growth of human pancreatic adenocarcinoma in *nu/nu* mice. In the enzyme group, the tumor mass increased up only to 47.6% of the control volume in the 30th day.

Conclusion: Although, the proteases were expected to have mainly the antimetastatic effect in cancer progression, these results confirm growth inhibition of primary tumor by trypsin, chymotrypsin and papain solution.

544 PUBLICATION

Gemcitabine (G) in combination radiationtherapy (RT) in stage III-IV pancreatic cancer: First results of a current Phase I study

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The purpose of the study was to determine the maximal tolerated dose (MTD) of G. in combination with radiation in patients with stage III/IV pancreatic cancer since it is known that G. is a potent radiation sensitizer of human pancreatic cells in vitro (Int. J. Radiat. Oncol. Biol. Phys. 34: 867, 1996). Also it has been reported, that dose of G. of 500 mg/m^2 might be a tolerable dose when G. was delivered concurrently to radiation (C.J. Mc Ginn ASCO 1998, Abstr. 1014).

Material and Method: The therapy encompassed a radiation of the primary tumor region and the lymphatic drainage paths up to the hilar region of the liver. A total dosage of 50.4 Gy was targeted based on a single dose per day of 1.8 Gy. The radiation was carried out on all patients on the basis of a continuous course and with a three-field-box technique. The volume of treatment amounted to 1–1.5 liters. G. was applied on days 1, 8, 15, 22 and 29. The radiation therapy followed one hour after the G. application (30 minute iv infusion.). The dose escalation started from 200 mg/m^2 and increased in 50 mg/m^2 steps, up to 350 mg/m^2. At each dose level a cohort of three patients were treated and increased to 6 patents when grade 3/4 hematological and non hematological toxicities appeared, except nausea, vomiting and hair loss.

Results: 16 patients have been entered the study so far. No grade 3/4 toxicity was found at dose level 1 of G. 200 mg/m^2 and at dose level 2, G 250 mg/m^2. Because of lack of significant toxicity it has been decided to enroll 2 patients on dose level 2. However, at dose level 3 (300 mg/m^2), grade 3 leukopenia was found in 2 out of 6 patients. Beside the hematological toxicity grade 1/2 nausea and vomiting was observed and 1 patient with grade 4 toxicity of ALT and AST.

Efficacy: At dose level of 200 mg/m^2 one patient was found as stable disease (SD), 2 patients progressed during therapy. 1 patient at this dose level is still alive after 8 month. At dose level 2 (250 mg/m^2) one patient progressed and one patient is still alive after completing the therapy. At dose level 3 (300 mg/m^2) all patients developed SD. Progression have been seen after 4 month, 3 month and 1 month respectively and 2 patients are still stable disease.

Currently 6 patient are enrolled on dose level 3 (350 mg/m^2). At this is dose level 2 patients developed Grade 3 and grade 4 leukopenia.

Conclusion: G. in combination with radiation shows a different MTD when given 1 hour before radiation. The study is still ongoing.

545 PUBLICATION

Gastric carcinoma: A phase II study of capecitabine with new dosing regimen in patients with advanced/metastatic gastric carcinoma

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Purpose: Capecitabine is a fluoropyrimidine carbamate with anti-neoplastic activity. It is an orally administered systemic prodrug of 5′-deoxy-5-fluorouridine (5′-DFUR) which is converted to 5-FU. We investigated efficacy and toxicity of capecitabine in advanced/metastatic gastric carcinoma patients.

Methods: Capecitabine was administered at a daily dose of 1657 mg/m^2 for 3-weeks followed by a 1-week rest period and given as 4-week cycles. This treatment dosing regimen was determined from its MTD (2510 mg/m^2) in continuous dosing of a phase 1 study in Japan. Eligibility criteria were as follows: 1) histologically/cytologically confirmed gastric carcinoma with measurable and/or evaluable lesions, 2) PS 0–2, 3) age <75, 4) prior chemotherapy no more than 1 regimen, 5) adequate bone marrow, liver, renal and cardiac functions, 6) written informed consent.

Results: Totally, Thirty-two patients were entered into a multi-center phase 2 study from July 1996 to December 1997. One patient was ineligible due to prior chemotherapy violation. Patient characteristics in 31 eligible cases were 22 males, 9 females, median age 61 (range 36–74). The number of treatment cycles ranged from 1 to 9. Overall response rate was 19.4% (95%CI 7.5–37.5%) in 31 eligible cases, and the response rate in patients without prior chemotherapy (including no chemotherapy in the adjuvant setting) was 24% (6/25). Only one NCIC CTC grade 3/4 related adverse event, increase in total bilirubin (grade 3, 6.3%) occurred in >5% of patients. Other related grade 3 adverse events were skin rash, increase in GOT, increase in blood sugar, decrease in hemoglobin & hematocrit, and increase in creatinine (each 3.1%). There was no other related grade 4 adverse events. Median survival time in eligible cases was 246 days (95%CI: 193–306+ days).

Conclusion: Oral administration of Capecitabine with the dose of 1657 mg/m^2 for 3-weeks-on and 1-week-off exhibits anti-tumor activity with a favorable safety profile and warrants further investigation.

546 PUBLICATION

Phase II study of gemcitabine (GEM) combined with radiation therapy (RT) in localized, unresectable pancreatic cancer

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Purpose: To evaluate the efficacy and safety of GEM combined with RT in patients (pts) with localized, unresectable pancreatic cancer.

Methods: Weekly GEM at a dose of 1000 mg/m" for seven weeks was given initially, in order to provide clinical benefit (CB) and to select non-progressing pts for entering into the chemoradiotherapy (CRT) phase of the treatment. This consisted of GEM 400 mg/m" weekly × 3 every 28 days for 2 cycles, delivered concurrently with RT to a total dose of 50.4 Gy in 1.8 Gy daily fractions. GEM dose was re-escalated to 1000 mg/m" after completion of RT.

Results: Between 8/97 and 12/98, 15 pts entered this study. Their median age was 65 y (38–84 y) and median performance status (PS) was 2 (1–3). Seven pts (46%) achieved positive CB response, measured by pain relief, improvement in PS or weight gain, and one pt was stable. Objectively, they had no tumor progression and thus enrolled to the CRT phase, followed by GEM alone. Five of them (33% of all pts) are alive and asymptomatic 10 m+ to 19 m+ after start of treatment, having objective partial response (2), minimal response (1) and no change (2). Overall median survival was