

disease. Starting dose (dose level 1) were docetaxel 50 mg/m² on day 1, fixed dose intravenously cisplatin (15 mg/m²/day) and continuous infusion 5-FU (800 mg/m²/day) on day 1–4. Nine patients received this combination chemotherapy (TPF) at the two different dose level. DLT was defined as follows (according to NCI-CTC version 2.0); Grade 4 neutropenia lasting for more than 4 days, Grade 4 anemia and thrombocytopenia, Grade 3 neutropenia accompanied fever ($\geq 38^{\circ}\text{C}$), and Grade 3 non-hematological toxicity (except for nausea, appetite loss, general fatigue). Maximal Tolerated Dose (MTD) is determined when the incidence of critical toxicity exceeds 50% at a certain dose level.

Results: MTD was dose level 2: docetaxel 60 mg/m², cisplatin 15 mg/m², and 5-fluorouracil 800 mg/m²/day. DLTs were diarrhea on level 1, and febrile neutropenia, diarrhea, and stomatitis on level 2. The major toxicity were Neutropenia (Grade 3 and 4, 56%), Leukocytopenia (Grade 3, 44%), Anemia (Grade 3, 11%), Diarrhea (Grade 3, 33%) and stomatitis (Grade 3, 11%). The overall response rate was 44.4% and recommend dose's response rate was 66.7%.

Conclusions: The recommended dose of docetaxel in this study was determined to be 50 mg/m². This combination chemotherapy of recommended dose appeared to be highly active with a response rate of 66.7% and to have acceptable toxicities. Phase II multicenter study has already started.

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PUBLICATION

Epirubicin, cisplatin and capecitabine for advanced biliary tract adenocarcinoma: a phase II study

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Background: Advanced biliary tract cancers (BTC) are associated with a very poor prognosis. Although numerous chemotherapeutic agents have been tested, the role of palliative chemotherapy in BTC has not yet been clarified. New therapeutic strategies are thus needed to improve the efficacy and survival, and we designed this study with new effective drug combination.

Materials and Methods: Patients with recurrent or metastatic BTC received a combination of epirubicin 50 mg/m², cisplatin 60 mg/m² on day 1, and capecitabine 1,000 mg/m² twice daily as an intermittent regimen of 2 weeks of treatment followed by a 1-week rest. Treatment was repeated every 3 weeks.

Results: Of 42 patients registered (14 with extrahepatic and 14 with intrahepatic cholangiocarcinoma, 6 with gallbladder cancer, 8 with ampulla of Vater cancer), one patient withdrew his consent and never received protocol therapy. The median age was 57 years (range, 36–69) and 5 had Zubrod performance status of 2. Objective responses were, which maintained for a median of 7 months), observed in 15 patients (36%) with 10 stable diseases. With a follow-up duration of 16 months, the median survival time was 8 months (95% confidence interval, 5–10 months). In total, 177 chemotherapy cycles were delivered, with a median of 5 cycles per patient (range, 0–9). Toxicity was mainly myelosuppression and mucositis. One patient died of hepatic failure between treatment cycles. For all patients, response to treatment was positively correlated with survival.

Conclusion: This combination chemotherapy with epirubicin, cisplatin and capecitabine feasibly offered promising antitumor activity in patients with advanced BTC.

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PUBLICATION

Irinotecan and gemcitabine (IrinoGem) combined with 3-D conformal radiation therapy for locally advanced pancreatic cancer

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Background: Chemoradiation for locally advanced pancreatic cancer may improve local control and long-term survival. The combination of irinotecan (Irino) and gemcitabine (Gem) (IrinoGem) is active in pancreatic cancer and has an acceptable toxicity profile (Rocha Lima et al, JCO, 2002). Both drugs are also radiosensitizers. Therefore, we conducted a phase I/II study to evaluate the feasibility and efficacy of IrinoGem combined with radiotherapy (RT) in patients (pts) with localized, unresectable pancreatic cancer.

Material and Methods: Pts received 2 induction cycles of Gem 1000 mg/m² and Irino 100 mg/m² administered on days 1 and 8 of each 3-week treatment cycle. This was followed by 3 cycles of low-dose IrinoGem with concurrent abdominal radiation. Gem was administered at a fixed dose of 300 mg/m² and doses of Irino were escalated in successive

cohorts from 20 mg/m² to 50 mg/m², by increments of 10 mg/m². RT was delivered by 3-D conformal technique to the pancreas and lymphatic drainage at 1.8 Gy daily fraction to a dose of 50.4 Gy.

Results: Sixteen pts entered the study between 11/2002 and 1/2004. Their median age was 66 y (range, 48–80 y) and performance status was 1/2 in 10/6 pts. All pts received 28 induction cycles and 11 pts continued with 33 cycles combined with RT. Treatment was stopped during the induction phase in 5 pts (toxicity 1, stent complications 1, refusal 1, tumor progression 2). Grade III–IV adverse events were diarrhea, vomiting, fatigue and mucositis in 5/16 (31%) pts during the induction phase and fatigue in 1/11 (9%) pts receiving concurrent chemotherapy and RT. There was no grade III–IV hematological toxicity. Thirteen pts were eligible for efficacy. Nine pts (70%) achieved clinical benefit response (CBR). One pt (8%) had an objective partial response, 7 pts (54%) had stable disease and 5 pts (38%) progressed, 2 of them during the induction phase. Release of major vessels encasement by the tumor was noticed in 2 pts, and one of them underwent R0 pancreatectomy. Median time to tumor progression was 6 m (range, 1–32+ m) and overall survival ranged from 2 to 32+ m, with a median of 13 m. Five pts are alive 1 y (1 pt), 2 y (3 pts) and 3 y (1 pt) after start of treatment.

Conclusions: This schedule of IrinoGem and RT is well tolerated and can provide CBR and disease control in pts with localized, unresectable carcinoma.

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PUBLICATION

Phase I/II study of S1 plus docetaxel in patients with advanced or recurrent gastric cancer

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Background: S1 and docetaxel (TXT) show significant single-agent efficacy in gastric cancer and are synergistic in vivo studies. We performed a phase I/II study of S1 and docetaxel combination chemotherapy to determine the maximum-tolerated dose (MTD), recommended dose (RD), and efficacy in unresectable or recurrent gastric cancer.

Methods: Docetaxel was administered intravenously on day 1 and S1 was administered orally on days 1–14. Treatment was repeated every 3 weeks. Doses of each drug in the phase I study were as follows: TXT/S1- level 1 60/60; level 2A 60/80; level 2B 75/60; level 3 75/80 (mg/m²). Phase II study is being conducted with RD based on the phase I study.

Results: Fifteen patients (median age 52) were enrolled in this phase I study and 9 patients (median age 52) were enrolled in this phase II study. No dose-limiting toxicities (DLTs) occurred at level 1, 2A, and 2B. At level 3, 2 of 3 (66.7%) patients developed DLTs (1 patient: grade 4 neutropenia with fever, 1 patient: grade 4 neutropenia with grade 3 stomatitis). Therefore, the dose at level 3 was determined as the MTD and the dose at level 2B was determined as the RD. The response rates of the phase I study were as follows: level 1 0% (0/3); level 2A 33.3% (1/3); level 2B (RD) 66.7% (4/6); level 3 66.7% (2/3). The response rate of the phase II study was 66.7% (4/6 evaluable patients: 1 CR, 3 PR, 1 SD, and 1 PD). Two patients (age 66 and 64 years old) developed fatal toxicity (grade 4 neutropenia with fever and shock) during the phase II study. The phase II study was well tolerated by the other 7 patients (all except 1 patient were younger than 60 years old). Additional phase I study with level 2A for the patients older than 60 years (n=3) was conducted. No DLTs occurred at this level and the toxicities were easily manageable.

Conclusion: Level 2B (TXT/S1 at 75/60 mg/m²) for the younger (<60 years old) patients and level 2A (TXT/S1 at 60/80 mg/m²) for the older patients are the RD of this combination chemotherapy. This combination regimen showed a high response rate and tolerable toxicities in patients with advanced or recurrent gastric cancer. The phase II study is now under way.

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PUBLICATION

Salvage surgery after failure of oncologic therapy for anal cancer

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Background: After primary oncologic therapy for epidermoid anal cancer some 20%–30% will have either residual disease or experience locoregional recurrence. Extensive surgical resection remains the only treatment with a possible curative outcome in these cases. We report the results in patients operated in our institution.

Material and Method: Retrospective assessment of patients operated for cure with abdominoperineal resection (APR) for residual or recurrent epidermoid anal cancer after primary oncologic therapy from 1990 through 2003.