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Weekly regimen of cisplatin (CDDP), epirubicin(EPI), fluorouracil (5FU) and folinic acid (FA) with G-CSF is active in advanced gastroesophageal(GE) and gastric(G) cancer: results of a phase II study

S. Palmeri, M.C. Macaluso, M. Vaglica, G. Modica, L. Di Noto, G. Di Vita, C. Sciumè, G. Vetri, E. Vassallo, G. Di Gesù. *Dipartimento di Discipline Chirurgiche ed Oncologiche, Università di Palermo, Palermo, Italy*

Background: We investigated the efficacy of an intensive weekly regimen in patients (pts) with advanced GE and G cancer in terms of response rate and improvement of the resectability rate.
Materials and methods: 28 pts with unresectable and/or metastatic GE or G cancer received a 1 d/week administration of CDDP 40 mg/m^2, 5-FU 500 mg/m^2, EPI 35 mg/m^2, FA 250 mg/m^2. From day 2 to 5, prophylactic G-CSF was given. After 8 weeks of therapy pts received a restaging of their disease. 16 pts had histologically confirmed diagnosis of G cancer, 12 GE cancer. 12 had locally advanced unresectable disease only; 7 had either primary unresected and metastatic disease (liver 1; nodes 2; peritoneum 2, lung 1; retroperitoneum 1); 5 had metastatic disease (peritoneum 3; retroperitoneum 1; lung 1) and primary tumor resected; 4 pts were treated in an adjuvant setting.
Results: so far 297 cycles have been administered, with a median of 9(2–26)/pt; (at time of writing) all pts were evaluable for toxicity (WHO) and 18 for response (WHO). The overall response rate was 61% with 1 pCR(6%) and 10 PR (55%). A SD was reported in 3 pts (17%) and a PD in 4 (22%). A clinical benefit (ORR+SD+ symptoms relief) was seen in 16/18pts (88%). 7 /12 pts, with only unresectable disease, underwent surgery and were completely resected with a post-chemo resectability rate of 58.3%. After surgery, 5 out of these 7 pts received the same regimen as adjuvant therapy. G3/4 toxicities were as follows: 43% pts neutropenia, 14% thrombocytopenia, 14% anaemia. Nausea/vomiting(14% G3/4) were the main non-hematologic toxicities. No treatment-related death was reported. The median survival of the whole population was 7.1 months (mo) (95% CI: 1.1–13.1). 4 pts lived >15 mo. The median survival in the responders' group and non responders pts was 12.7 (95% CI: 9.6–15.8) and 3.3 (95% CI:0–8.1) respectively (*P*001). In the resected pts the median survival was 12.7 mo (95% CI:10.4–15). Median time to progression was 7.1 mo (IC 95%:4.6–9.6) in all evaluable pts and 11.9 mo (IC95%:3–20.7) in resected pts. Median duration of response (14 pts) was 9.4 (IC 95%:3.7–15).
Conclusion: These data confirm the high activity and manageable toxicity of this weekly regimen. Of note is the very good resection rate (58.3%) observed in previously unresectable tumors. These data, although preliminary, suggest that this regimen may be investigated as a neoadjuvant therapy in the treatment of locally advanced G and GE cancer.

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Capecitabine and docetaxel in metastatic gastric cancer, an ongoing phase II study

P.C. Thuss-Patience[1], A. Kretzschmar[2], A. Loew[1], G. Massenkeil[1], D. Pink[2], B. Lebedinzew[1], S. Micheel[2], B. Dörken[1,2], P. Reichardt[1,2]. *[1]Charité, Campus Virchow-Klinikum, Med. Klinik m.S. Hämatologie u. Onkologie, Berlin, Germany; [2]Charité, Campus Buch, Robert-Rössle-Klinik, HELIOS-Kliniken Berlin-Buch, Hämatologie, Onkologie u. Tumorimmunologie, Berlin, Germany*

Introduction: Docetaxel shows promising activity as single agent and in chemotherapy combination regimens against gastric cancer. In a randomized phase II study it has been shown that the dual combination of docetaxel and continuous infusion 5-FU compared to the reference arm epirubicin, cisplatin and 5-FU (ECF) is a well tolerated and very active regimen (Thuss-Patience et. al. JCO 2005). In the current study we replace the 5-FU infusion with oral fluropyrimidines and evaluate the efficacy of the dual combination capecitabine and docetaxel (CapDoc). Here we report a preliminary analysis of this ongoing prospective multicenter phase II trial.
Methods: *Eligibility:* Metastatic or locally advanced gastro-esophageal junction or gastric adenocarcinoma, ECOG PS 0–2, no prior palliative chemotherapy. Chemotherapy: Docetaxel 75 mg/m^2 d1, capecitabine 2000 mg/m^2 d1–14, q3w.
Results: 29 patients (pts) are included in this ongoing trial. Data is available for 26 pts. Age: 32–79 years (median 61), M/F 18/8, ECOG PS 0: 6 pts, 1: 18 pts, 2: 2 pts. Number of organs involved by metastases: 1: 4 pts, 2: 7 pts, 3: 10 pts, 4: 4 pts, 5: 1 pts. Measurable disease (RECIST): 26 pts. 128 cycles of chemotherapy are administered so far. *Toxicity:* 23 pts are evaluable for toxicity (worst grade per patient; % of pts): Grade 1/2/3/4: Nausea: 48/9/–/– %, vomiting: 22/17/–/– %, diarrhea: 26/22/13/– %, asthenia: 33/46/4/– %, stomatitis: 9/22/17/– %, alopecia: 22/67/–/– %, fever or infection not neutropenic: 13/26/–/– %, neutropenic fever: -/–/9/– %, nail changes: 22/26/–/– %, atrial fibrillation: 4/9/–/– %, paresthesia: 9/9/–/– %, dizziness: 22/4/9/– %, hand–foot-syndrome: 30/9/26/– %, leuko-neutropenia: -/30/17/30%, thrombocytopenia: 17/–/–/– %, anemia: 38/13/9/– %, fluid retention: 17/–/–/-, pulmonary embolism: -/9/4/4, pneumonitis: -/4/–/-. Dose adjustments of docetaxel had to be made in 38% and of capecitabine in 50% of pts, respectively, during the course of therapy.
Response: 11 of 16 pts with tumor related symptoms showed a subjective improvement of symptoms (69%). 21 pts are so far evaluable for objective response: CR 1 pt, PR 9 pts, NC 9 pts, PD 2 pts, (objective response rate: 47.6%). The median time to tumor progression is 6.0 months. So far only 10% of patients showed primary resistance to CapDoc.
Conclusion: These preliminary data suggest that CapDoc is a well tolerated combination with very promising efficacy

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The experience of proton beam therapy for the patient with hepatocellular carcinoma

A. Kawaguchi, M. Murakami, Y. Oda, K. Kagawa, H. Mayahara, Y. Hishikawa, M. Abe. *Hyogo Ion Beam Medical Center, Radiology, Hyogo, Japan*

Background: Proton beam therapy (PBT) was started from May, 2001 in Hyogo Ion Beam Medical Center (HIBMC). Between May 2001 and April 2004, 27 patients with hepatocellular carcinoma (HCC) were treated with proton beams. This study is to evaluate the efficacy of PBT for the patient with HCC.
Materials and Methods: Eligibility criteria for the patient with HCC in HIBMC as following; solitary tumor, no ascites, performance status of 0 to 2 and no serious comorbidities other than liver cirrhosis. We classified the patient in two groups, Group A; with virus hepatitis, Group B; without virus hepatitis. The back ground of the patients were 23 male / 4 female, median age of 69 years, median size of tumor 39.5 mm in Group A and 19 male / 3 female, median age of 69 years, median size of tumor 71 mm in Group B and 4 male / 1 female. For the planning of PBT, a treatment planning system: FOCUS-M (Mitsubishi Co.) was used by a radiologist. The clinical target volume (CTV) included the gross tumor volume with a 5 to 10 mm margin in all directions by image fusion technique according to CT images and MR images. The planning target volume (PTV) of the initial field encompassed the CTV with a 5 to 8 mm margin. We added because of respiratory synchronization, the caudal margins: 1/3 mm respiratory movements measured by fluoroscopic examination. The accelerated energy of the proton beam is 150 or 190 MeV. The total dosage / fractions were 76 cobalt gray equivalent (GyE) / 20 fractions or 60 GyE / 10fractions. Median follow-up period was 20 months.
Results: Acute adverse effect (NCI-CTC ver. 2.0) was tolerated in all patients and PBT was completed as planned in all patients. In Group A, 59% of the patients showed the recurrence in the outside of irradiated field but local recurrence was not recognized. In Group B, no patients showed the recurrence in the outside of irradiated field, but only one patient who had maximum tumor size; 119 mm showed the local recurrence. Our results of PBT for the patient with HCC were; 1) the excellent local control, 2) no cure in Group A but the possible cure in Group B. According to this result, we should select the patients before treatment for the purpose of treatment.

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Proton beam therapy for hepatocellular carcinoma patients with severe cirrhosis

M. Hata[1], K. Tokuuye[1], S. Sugahara[1], K. Kagei[1], N. Fukumitsu[1], T. Hashimoto[1], K. Ohnishi[1], K. Ohara[1], Y. Matsuzaki[2], Y. Akine[1]. *[1]University of Tsukuba, Radiation Oncology, Tsukuba, Japan; [2]University of Tsukuba, Gastroenterology and Hepatology, Tsukuba, Japan*

Background: Hepatocellular carcinoma (HCC) patients with severe cirrhosis are usually treated with supportive care because of their poor prognosis. However, the survival of severe cirrhotic patients has currently improved due to advanced treatments. We performed a retrospective review to determine the role of proton beam therapy for HCC patients with severe cirrhosis.
Material and methods: Of 197 patients with HCC treated with proton beam therapy between November 1990 and January 2000, 19 patients had Child-Pugh class C cirrhosis. There were 14 men and 5 women and ages at proton beam irradiation ranged from 51 to 69 years (median 61). The hepatic tumors were solitary in 14 patients and multiple in 5, and the tumor size ranged from 25 to 80 mm (median 40) in maximum diameter. No patients had regional lymph node or distant metastasis. A total dose of 50–84 Gy (median 72) in 10–24 fractions was delivered to the tumors.
Results: All tumors but one treated with proton beam therapy were controlled at the median follow-up period of 16 months (range, 3–62). One patient had growth of the irradiated tumor and a new hepatic tumor outside