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Adjuvant gemcitabine (GEM) and concurrent irradiation can be safely administered after curative resection of pancreatic adenocarcinoma

A. Demols[1], J. Closset[1], F. Gay[1], S. Danhier[2], M. Colette[3], G. Houbiers[4], M.T. Closon[3], P. Van Houtte[2], J.L. Van Laethem[1]. [1] *Hôpital Erasme; [2] Institut Jules Bordet, Brussels; [3] CHU Sart Tilman, Liège; [4] CHR Seraing, Belgium*

Purpose: Chemoradiation using 5FU has not yet shown any benefit in the adjuvant setting of pancreatic cancer. Gemcitabine (GEM) has potential activity in advanced pancreatic cancer and is a potent radiosensitizer. We evaluate the feasibility of postoperative administration of GEM alone, followed by concurrent GEM and irradiation (RT) in patients after curative resection of pancreatic adenocarcinoma.

Methods: GEM 1000 mg/m^2 (D1 + D8 q 21 days for three courses) was given within 8 weeks after surgery and was followed by GEM 300 mg/m^2 weekly + split course RT (20 Gy/10 fractions × 2 course week with a two week rest). Total treatment time was 16 weeks. Seventeen patients (9 M/8 W; mean age: 53 range 42–74; PS 0–1) with stage II and III curatively resected pancreatic head adenocarcinoma were included.

Results: All patients had good recovery after duodenopancreatectomy. For GEM alone, all patients received the three planned courses with dose reductions (75% of the dose) in 5/17 patients (29%); all patients except two completed full chemoradiation; one received only 20 Gy due to WHO grade 4 vomiting and thrombopenia and the other stopped RT after 32 Gy due to early disease progression. No reduction in GEM during RT was necessary; no toxic death was noted; and WHO Grade 3/4 hematological and non hematological toxicities were 3/17 (17%) and 4/17 (nausea, vomiting) (23%), respectively. There was no late toxicity due to GEM/RT. After a median follow-up of 12 months, 10/17 patients are alive; two patients died from non disease related cause; DFS and OS were 8 and 12 months, respectively. One-year survival was 70%.

Conclusion: This adjuvant regimen is well tolerated and can be easily administered after curative surgery for pancreatic cancer. Intensification of such regimen with continuous irradiation and weekly Gemcitabine could deserve further investigation.

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90yttrium-labeled glass microspheres (therasphere) given to the hepatic artery for treatment of unresectable HCC: initial clinical experience

B. Carr, M. Sheetz, M. Brown, F. Torok, B. McCook, A. Zajko, L. Collins, M. France. *University of Pittsburgh Medical Center, Pittsburgh, USA*

Aim: 90Yttrium-glass microspheres have the potential for delivering high dose radiation to localized vascular hepatic tumors safely and economically. We plan to evaluate the safety and feasibility of this therapy in unresectable US patients (pts) with HCC, aiming to deliver 100-150Gy to either or both hepatic lobes for a max of 2 treatments.

Results: 14 pts have been treated since 10/2000, 6 had two cycles and 8 had one cycle of Rx and 9 are evaluable for response and all evaluable for toxicity.

Responses: 3/9 pts had a PR by CT. 5 pts had decreased vascularity, but no size change in tumor; 2 were stable and 1 developed lung mets. Median dose delivered was 124Gy per liver lobe (range 56-140). No acute hepato-toxicity was found. Several pts had minor and transient nausea. An additional 5 pts had Rx planning, but could not receive Rx due to vascular anomalies or lung shunting.

Conclusions: Therasphere appears to be a new, exciting, effective, safe and economic treatment for advanced stage HCC in this initial clinical experience. Accrual to this pilot experience is on-going.

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Randomized phase III study in advanced and metastatic pancreatic cancer: single-agent gemcitabine versus gemcitabine plus cisplatin

V. Heinemann[1], D. Quietzsch[2], H. Schoenekaes[3], F. Gieseler[4], H. Neuhaus[5], M. Szymala[1], W. Hiddemann[1], A. Schalhorn[1]. [1] *Klinikum Grosshadern, Med. Clinic III, Munich, Germany; [2] Klinikum Chemnitz, Chemnitz, Germany; [3] Klinikum Nuernberg Nord, Nuernberg, Germany; [4] University Clinic Kiel, Kiel, Germany; [5] Staedtische Kliniken Darmstadt, Darmstadt, Germany*

Treatment of advanced and metastatic pancreatic cancer with gemcitabine (GEM) and cisplatin (CIS) was shown to be effective in a phase II trial (Heinemann, ASCO 1999) and induced response rates and survial times greater than those observed with GEM alone (Burris, JCO 1997). The present phase III trial was performed to compare efficacy and clinical benefit of the GEM/CIS combination to single-agent GEM. Pts received either GEM 1000mg/m2 plus CIS 50mg/m2 on days 1 and 15 of a 28-day schedule (arm A) or GEM 1000 mg/m2 on days 1, 8, and 15 of a 28-day schedule (arm B). Of 170 planned pts, 169 pts with histologically documented cancer of the pancreas have been enrolled. Hundred pts are presently evaluable for toxicity: arm A: 46 (m/f = 30/16), arm B: 54 m/f = 33/21). Distribution of parameters between arms A and B are as follows: median age 57 yrs (range 40-78 yrs) vs 62 yrs (range 44-72yrs), median Karnofsky PS 70% (range 70-100%) vs 70% (range 70-100%), stage III 18% vs 18%, stage IV 82% vs 82%. Metastases were located in the liver 78% vs 72%. The median number of cycles administered was four in arm A (range 1-9) and 3.3 in arm B (range 1-11). WHO Grade 3/4 toxicities (per patient analysis) in arms A and B included: anemia 13% vs 9.2%, leucopenia 13% vs 5.5%, thrombopenia 8.6% vs 7.4%, elevation of bilirubin 4,4% vs 5.5%, alkaline phosphatase 4,3% vs 5.5%, transaminases 0% vs.3,7%, mucositis 4,3% vs 3,7%, nausea and vomiting G3 33% vs 3.7%, and diarrhea 10.8% vs 7.4%. In conclusion: treatment of advanced pancreatic cancer with GEM/CIS or with GEM is - appart from nausea and vomiting - comparably well tolerated.

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Phase II trial of Alimta plus Gemzar administered every 21 days in patients with advanced pancreatic cancer

H. Kindler[1], D. Strickland[2], W. Dugan[3], J. Visconti[4], J. Liebman[5], H. Hochster, A. Jacobs, J. Kugler, W. John. [1] *University of Chicago, Chicago, IL, USA; [2] Memphis Cancer Center, Memphis, TN, USA; [3] Indiana Onco-Hem Consultants, Indianapolis, IN, USA; [4] St. Louis University, St. Louis, MO, USA; [5] Onc/Hem Consultants, Albuquerque, NM, USA*

Alimta (pemetrexed disodium), a multi-targeted antifolate that inhibits TS, DHFR, and GARFT, has activity in pancreatic cancer (Ann Oncol 11:101; 2000). The combination Alimta/Gemzar (gemcitabine HCL) is synergistic in vitro and broadly active in a phase I trial (JCO 18:1748, 2000). We evaluated the combination of Alimta and Gemzar in a multicenter phase II trial in previously untreated pts with histologically proven unresectable pancreatic cancer. Gemzar 1250 mg/m2 was administered over 30 minutes on days 1 and 8 of a 21-day cycle. Alimta 500 mg/m2 was given over 10 minutes on day 8. CT scans were obtained every 2 cycles. Clinical benefit response was assessed weekly. Folate/B12 supplementation was initiated in 11/99, when safety data showed that it significantly decreases toxicity. 39 eligible pts enrolled 9/99-11/00. Pt characteristics: male 62%; median age 61 (range 37-81); Karnofsky PS 100 5%, 90 56%, 80 36%, 70 3%; metastatic disease 95%; prior adjuvant 5-FU 10%. Results: 131 cycles were delivered (range 1-7, median 3). There were 5 partial responses (PR) (overall response rate 12.8%). Another PR has not yet been confirmed. Stable disease 59%; progressive disease 15.4%. Median time to progression: 3.6 months. Survival data will be presented. Of 29 pts eligible for clinical benefit assessment, PS improved in 8% and stabilized in 72%. Weight increased in 4% of pts and stabilized in 68%. Grade 3/4 hematologic toxicities (%pts): neutropenia 74%; leukopenia 56%; neutropenic fever 8%; anemia 10%; thrombocytopenia 13%. Grade 3/4 nonhematologic toxicities: elevated transaminases 18%, decreased creatinine clearance 16%. Conclusion: the combination of Alimta plus Gemzar is active in advanced pancreatic cancer, with acceptable toxicity.