562 POSTER

HIGH DOSES OF EPIRUBICIN AND 5-FLUOROURACIL WITH OR WITHOUT CISPLATIN IN ADVANCED GASTRIC CANCER

A. Roth, K. Kolarić, D. Županc
University Hospital for Tumors, Zagreb, Croatia

From Sept. 1991. to Jan. 1995. 80 pts. with advanced gastric cancer entered phase III clinical trial. The aim of the study was to determine activity of high doses of 5-fluorouracil and epirubicin (FE) vs. the same combination + cisplatin (FEP) in that group of pts. Out of 80 pts. 73 were evaluable. The treatment involved in FE arm 120 mg/m^2 of epirubicin i.v. on day 1 and 1000 mg/m^2 in 6-hour infusion of 5-fluorouracil on days 1, 2, 3, 4, 5: in FEP arm the same combination + cisplatin 30 mg/m^2 on days 2.4 was administered. The cycles were repeated after 4 weeks. In FE arm 37 pts. were evaluable with 10 partial and 1 complete remission (29.7%), in FEP arm out of 36 pts. 14 partial and 1 complete remission (41.7%) were observed. Median survival in FE group was 6.3 mos, and in FEP group 8.1 mos. Differences were not statistically significant. Toxicity was tolerable and reversible. Our trial being still under way, the final results will provide a more accurate answer with regard to the value of the two administered protocols.

563 POSTER

EFFICACY OF THE COMBINATION OF ETOPOSIDE (E) AND CISPLATINUM (P) IN THE TREATMENT OF NEUROENDOCRIN DIGESTIVE CARCINOMA (NEC)

K. Yakendji, Ph. Rougier, M. Ducreux, P. Duvillard, M.C. Fabri, Ph. Lasser, J.P. Armand
Institut Gustave-Roussy, Unité La Grange, rue Camille Desmoulins 94805 Villejuif, France

Combination of E and P has shown high response rate in NEC. A pilot study was performed to study the tolerance and efficacy of a new combination ore 120 mg/m^2 day 1 to 3 and P 100 mg/m^2 day 2 every 3 or 4 weeks in the treatment of these patients (pts). 16 pts (male/women: 12/4) have been enrolled. Median age was 46 years. Performance status was <2 in 13 pts. Primary was pancreatic in 10, small bowel in 4, gastric in one and of unknown primary in 1. Metastases were found in 12 pts with liver involved in 8. A poorly differentiated carcinoma was found in 11. A carcinoid secretion was found in 5. Surgery and/or chemotherapy had been performed in 12. 16 pts received 76 cycles (c) (median 5). *Results:* Toxicity: mainly haematological: grade 3 and 4 granulocytopenia in 17 and 18 cycles (2 neutropenic fever), grade 3–4 thrombocytopenia (5 c), grade 4 emesis (7 c), grade 1–2 neurologic (7 c) and grade 1–2 renal (2 c). *Response Rate:* 8/16 PR (50%) with 6/11 in poorly differentiated. NEC, 5 SD and 3 PD. Median duration of response was 7.3 month. Median survival was 10 months. A complete resection was performed in 1. *Conclusion:* Administration of E and P with these doses and schedule result in high response rate with an easily manageable toxicity.

564 POSTER

LITHIUM GAMMOLINOLENATE (LIGLA)- A NOVEL OUTPATIENT TREATMENT FOR NONRESECTABLE PANCREATIC CARCINOMA (PC)

C.R. Underhill[1], P.G. Harper[1], M.S. Highley[1], J. Ahem[1], S.C. Barker, C.J. Wright[1], A. Ahmed[1], S.J. Houston[1], D.W. Miles[1], M. Larvin[2], R.C. Mason[3]
[1]Department Med Oncology
[3]Department Surgery, Guys Hospital, London SE1 9RT
[2]Department Surgery, Lewisham Hospital, London, SE13 6LH, U.K.

LiGLA, a lithium salt of an essential fatty acid, has cytotoxicity *in vitro* and *in vivo* against a number of tumour types; a phase II trial has shown median survival of 410 days in patients (pts) with advanced, non-metastatic PC. As part of an ongoing multi-centre randomised phase III study, we have assessed, in a cohort of 6 pts, the feasibility of a short outpatient daily infusion, as compared to the usual inpatient continuous infusion for 10–14 days. All pts had histologically proven non-resectable PC. Karnofsky score >70%, assessable for toxicity & response, & no previous chemotherapy. The maximum period of infusion, via an indwelling. CVC, was 6 hours. Dose escalation was limited by short-lived macroscopic haemoglobinuria (due to an osmotic effect of LiGLA on erythrocytes), which developed at a dose level above 7 g/day. Total dose for each pt (determined by body weight) was 26–84 g. Days of infusion varied from 6 to 16. One pt experienced grade II anaemia. No other toxicities were seen (in particular no renal or Lithium toxicity). This method has a similar toxicity profile to the inpatient infusion. No meaningful comment can be made on efficacy equivalence. Short term infusion should be considered in future trials of this interesting, novel agent. The future development of an ambulatory pump protocol offers a potential home based treatment.

565 POSTER

PHASE II STUDIES WITH EO9 IN BREAST, COLORECTAL, GASTRIC, PANCREATIC AND NSCLC

J. Wanders[1], N. Pavlidis[2], T. Gamucci[2], W.W. ten Bokkel Huinink[2], L. Dirix[2], I. Wolff[2], J. Verweij[2]
[1]EORTC-New Drug Development Office
[2]EORTC-Early Clinical Trials Group (ECTG)

EO9 is 8 bioreductive alkylating indoloquinone causing single strand DNA breaks after reduction by DT-diaphorase, with 8 broad spectrum of activity in preclinical studies. In Phase I studies the DLT was proteinuria and renal toxicity at 27 mg/m^2 in the 3-weekly schedule and 15 mg/m^2 in the weekly schedule. The ECTG performed Phase II studies in breast (B), colorectal (C), gastric (G) and pancreatic (P) cancer at the recommended dose of 12 mg/m^2/wk and 1 Phase II in NSCLC (N), randomizing for treatment with 22 mg/m^2 q3wks vs. 12 mg/m^2/wk. Between June 1994 and March 1995 131 patients (pts) were entered in the studies: 22 in B, 28 in C, 20 in G, 24 in P and 39 in N. 1 prior chemotherapy regimen was allowed for B, adjuvant treatment >1 year ago for C. All other tumor types had no prior chemotherapy. The median age of all pts was 59 (range 32–83), median PS 1 (range 0–2). 559 courses (33 of which in the 3 wkly schedule) have been evaluated for toxicity (using NCI-CTC grading). Main toxicities observed were nausea and vomiting (27 and 13% respectively), asthenia (28%), proteinuria (39%), creatinine elevation occurred in 3% of all crs. Proteinuria was more frequent (52%) in the 3-wkly schedule, and 1 episode of a gr.4 creatinine increase occurred in this study arm. Apart from 1 pt with severe fluid retention and renal toxicity with associated symptoms no gr.4 toxicities, and hardly any gr.3 toxicities were seen. So far no responses have been observed in 104 evaluated patients.

566 PUBLICATION

CELL PROLIFERATION IN EXOCRINE PANCREAS OF CARCINOGEN-TREATED RATS AND HAMSTERS

M.J. Appel, R.A. Woutersen
TNO-Nutrition and Food Research Institute, PO Box 360, 3700 AJ Zeist, The Netherlands

Cell proliferation in normal pancreatic tissue of saline-treated rats and hamsters and in putative preneoplastic pancreatic tissue of azaserine-treated rats and of N-nitrosobis (2-oxopropyl) amine (BOP)-treated hamsters was determined at 2, 6, 12, 26 and 52 weeks post-treatment. *Rats:* The BrdU Labeling Index (LI) in normal acinar pancreatic cells showed a time-related decrease. The LI in hyperplastic acinar loci was significantly higher than in normal acinar tissue. *Hamsters:* BOP-treatment caused a significant increase in the LI in pancreatic acinar cells. The LI in ductular cells was significantly higher in BOP-treated animals than in saline-treated animals 2 weeks post-treatment, but similar, thereafter. The LI in centroacinar cells was significantly higher in BOP-treated hamsters 2 and 26 weeks post-treatment. Cell proliferation was higher in tubular ductular complexes (lesions with a high potential for malignant transformation) than in cystic ductal complexes (lesions with a low potential to develop to ductular adenocarcinomas). Cell proliferation was highest in borderline lesions (lesions characterized by atypia, desmoplasia and inflammatory cells). It is concluded that determination of cell proliferation provides an easily quantifiable parameter to discriminate between putative preneoplastic lesions with a high or low growth potential, hence with a high or low potential to develop into carcinomas.

567 PUBLICATION

RETROSPECTIVE COMPARISON OF R1 AND R2–R3 GASTRECTOMY FOR CURATIVE GASTRIC CANCER

A. Arak, K. Kull, J. Lehtola, J. Mäkelä, H. Tuominen
Hospital of Oncology, Tartu, Estonia
Oulu University Hospital, Oulu, Finland

The benefit of R1-gastrectomy used in Oulu on 88 pts. (radicality 43.3%) and gastrectomy with extended (R2–R3) lymphadenectomy used in Tartu on 210 patients (pts.) (radicality 60.9%) during the 5-year period from 1983 to 1987 is compared. Although the 5-year survival rates were similar (45.5% in Oulu and 48.1% in Tartu), the comparative data of prognostic factors differed significantly ($P < 0.05$) in T stages, N stages and Borrmann types. The patients in Tartu had higher incidence