207 POSTER

Radiochemotherapy (RCT) of locally advanced oesophageal cancer – preoperative RCT vs. definitive RCT alone

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Background: Since 7-96 neoadjuvant RCT has been performed at the University Hospital in Dresden, Germany for selected patients (pts.) with locally advanced oesophageal cancer without distant metastasis.

A retrospective comparison of preoperative RCT vs. definitive RCT alone will be presented to compare the efficacy of both treatment strategies.

Material and methods: Between 9-95 and 10-02 131 pts. have been treated in a curative setting. 61 with preoperative RCT and 70 with definitive RCT. Preoperatively 40 Gy have been administered. Pts. being further inoperable or pts. with definitive RCT received 60 - 66 Gy. Simultaneous chemotherapy consisted in CDDP and 5-FU. The main endpoint of this analysis was overall survival.

Results: According to overall survival no significant difference in this intent-to-treat analysis was observed between preoperative and definitive RCT: 303 days vs. 315 days (Fig. 1).

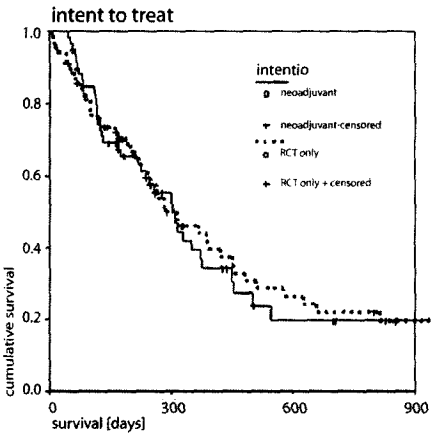

Fig. 1. "Intent to treat" analysis of 131 pts. with advanced oesophageal cancer treated with preoperative RCT or RCT alone.

27 of 61 pts. (44%) were successfully operated after preoperative RCT. Pts. treated with neoadjuvant RCT according to protocol had a higher 2-years survival rate compared to pts. got definitive RCT (42% vs. 28%, Fig. 2). However, this difference is not significant (p=0,26, log-rank). Pts. not eligible to receive successful surgery had a much poorer survival, although they received a cumulative dose of 66 Gy.

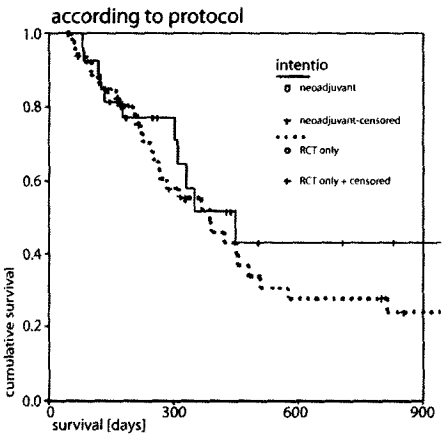

Fig. 2. Survival of 78 pts. treated "according to protocol" either with preoperative RCT or RCT alone.

Conclusions: The decision process for pts. with locally advanced oesophageal carcinoma receiving a preoperative RCT needs to be carefully evaluated. This is demonstrated by the fact that pts. who did not receive surgery had a poorer survival in this concept compared with pts. treated with RCT alone. An intensive interdisciplinary approach with high surgery competence of the centre is mandatory.

208 POSTER

Chemoradiotherapy after surgery for adenocarcinoma of the stomach. Final results of a prospective, phase II, single-institutional program

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Background: To evaluate the effect of surgery plus postoperative (adjuvant) chemoradiotherapy on the survival of patients with resectable adenocarcinoma of the stomach., we begun at the Hospital of Navarre in 1993, a phase II prospective study.

Material and methods: Forty six patients with pathological N+ or T3-T4 gastric cancer, were treated with postgastrectomy chemoradiotherapy. There were 33 men, and 13 women. By stage, there were 5 p. stage IB (11%), 9 p. stage II (19.5%), 12 p. stage III-A (26%), 9 p. stage IIIB (19.5%), and 11 p. stage IV (24%). R0 gastrectomy 37 p. (80%), R1 (residual microscopic disease) 8 p.(17%), and 1 p. had R2 resection. Treatment were similar than the used by Macdonald trial (1), and consisted of 425 mg of fluorouracil per square meter of body-surface area per day, plus 20 mg of leucovorin per square meter per day, for five days, followed by 4500 cGy of radiation at 180 cGy per day, given five days per week for five weeks, with modified doses of fluorouracil and leucovorin on the first four and the last three days of radiotherapy. One month after the completion of radiotherapy, two five-days cycles of fluorouracil (425 mg per square meter per day) and leucovorin were given one month apart.

Results: With median follow-up of 96 months, the median overall survival was 46 months. Five-years overall survival was 45%, and 5-Years specific-survival was 54%. Local recurrence occurred in 23% of the patients, and regional or distant metastases in 40%.

Toxicities: grade 3-4 toxic effects occurred in 16 p. (35%). Cumulative hematological toxicity precluded full chemotherapy in 9p (20%). There were not any toxic-related death.

Conclusion: In our series, patients with T2N0 stage were excluded for treatment. Nevertheless, our results are similar to the ones published by MacDonald, and it indicates that this combined treatment- now standard treatment for gastric cancer- can be administered safely in a Tertiary Hospital, and also that the results of the Intergroup can be reproduced in the clinical practice.

Reference

[1] Macdonald JS, Smalley SR, Benedetti J, et al: chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med,345:725-29; 2001.

209 POSTER

Treatment of pancreatic tumour cells with IC261 and spindle poisons alone or in combination leads to different effects on cell growth

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Background: For patients with advanced pancreatic cancer the established chemotherapies did not extend the median survival beyond several months. New approaches have to be developed. It has been shown, that the inhibition of Casein kinase 1 Delta (CK1δ) has similar inhibitory effects on the growth behaviour on tumour cells as spindle poisons.

Methods: Panc Tu 1 and Panc 89 cells were either treated with the CKId specific inhibitor IC261, the spindle poisons nocodazol and taxol, alone or in combination were analysed by FACS analysis at different time points. Additionally, RNA and protein levels of various proteins involved in cell cycle control and apoptosis were analysed by TaqManTM and Western Blot analysis, respectively.

Results: Our FACS analysis of different pancreatic tumour cells treated with IC261, nocodazol or taxol at different time points revealed a cell cycle arrest for IC261 or nocodazol treatment, whereas in the case of