

of T3-T4 tumors. No patients with T4 or N2-N3 tumors were operated on with curative intent in Oulu. The distribution of expansive: infiltrative Borrmann types was 4:1 (Oulu) and 1:1 (Tartu). Differences in the 5-year survival rates were noticeable ( $P < 0.05$ ) in more advanced stages (T3-T4, N2-N3, Borrmann III-IV types).

We may conclude that these differences can be explained by the more aggressive approach to the gastric cancer surgery in Tartu, specially in patients with advanced tumors. Otherwise the pts. in Oulu are more carefully selected for curative surgery than the pts. in Tartu.

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PUBLICATION

# **COMBINED CHEMORADIATION FOR ANAL CANCER: REPORT OF 22 CASES**

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From 1988 to 1994 22 patients (pts) with anal cancer, 16 females and 6 males, were treated with concurrent CT and RT as definitive therapy. Median age was 64 years (range 39-91). Hystotype was squamous carcinoma in 19 and cloacogenic carcinoma in 3 pts. Distribution per stage was: II 12, IIIA 3, IIIB 3; 4/22 cases were treated after surgical relapse (3 local, 1 inguinal nodal).

CT and RT started the same day. CT, modified from the schedule of Nigro, was: 5-FU 1000 mg/m<sup>2</sup>/day for 5 days by continuous, Mitomycin 10-15 mg/m<sup>2</sup> day 1, every 4 weeks. In 11/22 pts 5-FU was administered via a portable infusion pump. RT was delivered 1.8 Gy/day, 5 fractions/week, with a 6 MeV linear accelerator. A median dose of 45 Gy (40-50 Gy) was delivered on the anoperineal volume and the middle and lower pelvis, including bilateral inguinal and external iliac nodes, by opposite anteroposterior portals; after a median split of 10 days, a boost dose was given to the anoperineal region with a direct field by an electron beam of 9-16 MeV, up to a median total dose of 56 Gy (51-63 Gy). The same boost was given to metastatic inguinal nodes.

Nineteen pts completed the treatment and are evaluable for response and toxicity; 3 are still on therapy. Fourteen out of 19 pts received two cycles of CT, 5/19 three or more cycles. Pathologic response was documented in all the pts; pCR was achieved in 100% of cases. With a median follow-up of 19 months (range 5-78), 17/19 pts (89.5%) are free from relapse with maintained anorectal function. Two pts (10.5%) relapsed locally, after 8 and 11 months respectively; in one case abdominoperineal resection was performed as salvage therapy, and the pt is now alive NED; the other pt is receiving further CT.

Eleven pts (58%) had G3-WHO dermatitis; G3-4 systemic toxicity was uncommon: 2 thrombocytopenia, 1 neutropenia, 1 stomatitis. One pt had an impairment of a previous known angina pectoris. Late toxicity occurred until now in 2 pts, with a vaginal stenosis and a rectal stenosis. No difference in toxicity was observed in pts receiving 5-FU by pump.

The treatment was administered, with a 20% reduction of doses of chemotherapy, also to elderly pts (4 pts were  $\geq 75$  years), with good tolerance.

Although the period of follow-up is short, our study confirms that concurrent CT-RT is the standard treatment for anal cancer, with relevant but acceptable toxicity; the treatment is feasible and safe also in elderly pts.

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PUBLICATION

# **CONTINUOUS FLUOROURACIL INFUSION PLUS ORAL L-LEUCOVORIN AND ORAL ETOPOSIDE IN ADVANCED GASTRIC CANCER**

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Gastric carcinoma is considered moderately chemosensitive, but an effective chemotherapy regimen has not yet been found. Encouraging results in terms of activity and tolerability have been reported with a combination of i.v. leucovorin, fluorouracil and etoposide. However, etoposide and fluorouracil have demonstrated a schedule-dependency with high activity for the former when administered orally and for the latter when administered as a continuous infusion. In order to improve clinical results, we tested the activity and feasibility of the following combination: oral L-leucovorin, 5 mg/m<sup>2</sup> days 1-14; oral etoposide, 50 mg/m<sup>2</sup>; fluorouracil, given by continuous infusion days 1-14; cycles repeated every 28 days. A total of 20 patients has been enrolled, and 16 are evaluable for response and toxicity (for 4 it is too early). Patient characteristics were as follows: male/female, 11/5; median age, 62 years (range, 49-72);

performance status, 0-2; pretreated with surgery/adjuvant chemotherapy, 13/5. Sites of metastasis: 8 liver, 3 lung, 7 lymph nodes, 7 peritoneal carcinomatosis. A total of 52 cycles has been delivered (median/patient, 3 cycles). One complete remission (6%), 6 partial remissions (35%), 4 stabilizations of disease, and 5 progressions have been observed, for an overall response rate of 41%. Median duration of response was 6 months (range, 2-8+) and median time to disease progression was 4 months. No toxic death or grade III-IV toxicity has been observed. Mild or moderate side effects included mucositis (18%), diarrhea (12%) and leukopenia (18%). In conclusion, our preliminary results indicate that the schedule is safe well tolerated and highly effective in advanced gastric cancer.

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PUBLICATION

# **THP ADRIAMYCIN (THP): A PALLIATIVE TREATMENT OF LOCAL ADVANCED NON OPERABLE HEPATOCELLULAR CARCINOMA (HCC)**

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From 01/91 to 07/94, 20 patients (pts) with non operable HCC and alcoholic liver cirrhosis were treated by THP infusion. The pts were of median age 67 (49-82) years and WHO PS 2 (11) and 3 (9). All tumors were  $\geq$  or = to T3. All liver cirrhosis were Child B or C. *Regimen* was: D1 to D3 THP 20 mg. sqm, 30 mn infusion, Q 4 weeks. Treatment was stopped in cases of appearance of major progression, non manageable toxicity or complete response superior to 6 months. The median number of cycles delivered per pt was 10 (5-26) with a total of 243 cycles.

*Toxicity* was mainly hematological with neutropenia WHO grade (Gr) III 15%, Gr IV 2%, thrombopenia Gr III 3%, anemia Gr III 1.2%. No cardiac or renal toxicity was observed nor alopecia. Cycles were delayed for 1 week in 4% of cases and a reduction in dose was made in 9%, both for hematological toxicity. There was no septic complication nor hemorrhage.

*CT Scan evaluation* after 5 cycles showed PD in 7 pts (35%), SD in 5 pts (25%), MR in 1, PR in 4 (20%) and CR in 3 pts (15%). Out of these 3 CR 1 pt had a liver transplantation and died of post-operative complications and the other 2 have a continuing response with 8 and 13 months of follow up after finishing treatment. Ten pts had a high pre-treatment alpha foeto protein value. For 5 of these this value decreased, becoming normal in 2 cases, and for the other 5 pts this value increased. Overall median survival was 15 months (5-40). Eleven pts died and 9 are still alive with a median survival of 20 months (9-40).

THP infusion seems to be a good palliative treatment for these poor prognostic HCC with low hematological toxicity, no cardiac toxicity and an objective overall response rate of 35%

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PUBLICATION

# **EXTERNAL RADIOTHERAPY AND INTRALUMINAL BRACHYTHERAPY IN ADVANCED STAGES ESOPHAGAL CARCINOMA**

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The treatment for patients with advanced stages esophageal carcinoma should be aimed at maintenance of local control by means of saving esophageal passage, improving dysphagia and oral nutrition and preventing aspiration pneumonia as these sorts of complications are fatal. In this study, it was performed 15-16 Gy high dose rate intraluminal brachytherapy in 3 fraction preceded by 46-48 Gy external radiotherapy to 14 advanced stage inoperable patient in order not to exceed tolerable doses of the neighbouring tissues while maintaining efficient local control by radiation. Seven patients received neoadjuvant chemotherapy. Patients were assessed symptomatically, endoscopically and radiologically every 3 months after completion of treatment. Before treatment 6 patients could not take and 8 patients received only fluid food. We achieved symptomatic palliation in all of the patients. Endoscopically it was founded no macroscopic tumor in 6 patients, 1-2 cm tumor in 4 patients and bigger than 2 cm in 4 patients 3 months after treatment. Seven patients had distant metastasis. Survival was between 5-18 (mean 10 months). We did not observe radiation ulcer. External radiotherapy plus intraluminal brachytherapy is effective and safe for obtaining local control in advanced disease esophageal carcinoma.