was evaluated in a multicenter phase II study. Patients and treatment: 56 chemotherapy-naive patients with locally advanced or metastatic disease were enrolled. The median age was 60 years; men were 34 and women 22; PS was 0 (n = 15 pts), 1 (n = 21 pts) and 2 (n = 20 pts). G (1000 mg/m$^2$) was administered on day 1 and 8 and D (100 mg/m$^2$) on day 8, every 3 weeks; G-CSF (150 igr/m$^2$, sc) was given (day 9–15).

**Results:** All patients were evaluable for toxicity and 43 of them for response. Five (11.6%) pts achieved PR while 17 pts (39.5%) had SD and 21 pts (48.8%) PD. The median duration of response and the median TTP were 3 and 9 months respectively while the median survival was 8 months and the probability for one year survival 32%. Grade 3/4 neutropenia occurred in 15 pts (23%) and in 6 (11%) of them it was complicated with fever; 1 septic death occurred. Grade 3 anemia and grade 3/4 thrombocytopenia occurred in 6 (10.7%) and 4 (8%) pts respectively. Non hematologic toxicity: grade 3/4 diarrhea in 2 pts (4%), grade 2 neurotoxicity in 3 pts (5.4%) and grade 3/4 fatigue in 7 pts (13%); moderate hypersensitivity reactions in 4 pts (7.1%) and moderate fluid-retention syndrome in 14 pts (25%). A total of 201 cycles were administered (median number/patient: 3). The median administered dose was 90% and 94% of the planned doses for D and G, respectively.

**Conclusions:** Although, the D + G combination is well tolerated and seems to have a marginal activity in patients with advanced pancreatic cancer, conferring to them some clinical benefit, it does not seem to be superior to single-agent therapy with either G or D.

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## Direct endoscopic injection of cisplatin/adrenaline gel for palliation of dysphagia in patients with advanced esophageal cancer

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**Purpose:** We evaluated the safety and efficacy of direct endoscopic injection of cisplatin/adrenaline [epinephrine] injectable gel (CDDP/epi gel) for sustained local chemotherapy in the palliation of dysphagia in advanced esophageal cancer.

**Methods:** Open-label, Phase III studies enrolled patients with advanced esophageal cancer. CDDP/epi gel was injected intratumorally weekly for up to 6 wk or until all exophytic tumor was ablated.

**Results:** 23 patients enrolled; 17 evaluable. Median dysphagia grade: 3 (scale, 1–5; range 2–5). Median no. of treatments: 3 (1–6). Evaluations follow:

| Evaluation | Dysphagia[a] | Duration, days (median [range]) | Lumen Patency | Duration, days (median [range]) |
|---|---|---|---|---|
| Improved[b] | 3 patients | 55 (43–56) | 5 patients | 46 (36–56) |
| Unchanged | 9 patients | 39 (28–111) | 11 patients | 29 (28–111) |
| Worsened | 3 patients | – | 1 patient | – |

[a]Not available in 2 patients; [b]>1 point improvement.

Median survival for all 17 patients from first treatment was 146 d (44–301 d). The 5 patients with sustained tumor-volume reductions had a median survival of 242 d (158–301 d). No medically significant toxicities typically associated with systemic administration of cisplatin were reported.

**Conclusion:** Intratumoral CDDP/epi injectable gel is a simple method for relieving dysphagia due to predominantly exophytic esophageal cancer. This local chemotherapy may be complementary to stent insertion.

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## Radiochemotherapy in anal canal carcinoma (ACC). A randomized clinical trial comparing FluoroUracil-Cisplatinum (5FU-CDDP) and CDDP alone

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**Purpose:** 5 FU-CDDP and 5FU-Mitomycin are the most commonly used chemotherapy regimens for ACC in combination wih radiotherapy (RT). CDDP is also an attractive drug due to its high rate of clinical response in squamous cell carnicoma. This randomized trial aimed at comparing 5FU-CDDP versus CDPP given concomitantly with RT in ACC.

**Methods:** Between 1992 and 1995, 26 patients (pts) were included in this randomized trial. Inclusion criteria were: squamous cell carcinoma of ACC, without distant metastases, patients who could receive RT and chemotherapy for curative intent. Radiotherapy was given with external beam RT (direct perineal field: 30 Gy/10 F/12 days and sacral fields 18 Gy/6 F/3 weeks) followed by Iridium implant (15–25 Gy/1–2 days). One course of chemotherapy was given during EBRT: 5FU J1J4: 800 mg/m$^2$ continuous infusion CDDP: 80 mg/m$^2$ J2 (5FU-CDDP) or CDDP J1–J3: 30 mg/m$^2$ continuous infusion (CDDP alone).

**Results:** the two groups were identical sex ratios (11 female vs 2 male) median age (65 vs 66 years). T1-2 (9 vs 10) T3-4 (4 vs 3). NO (7 vs 6). N1-2-3 (6 vs 7). Median followup was 52 months. Two months alter the end of treatment a complete remission was seen in 11 pts in 5FU-CDDP group (I) vs 12 pts in CDDP group (II). There was no local recurrence in group I and one in group II. At 4 years the overall survival was 91% in both groups. There was 2 grade 3 complications in group I and none in group II.

**Conclusion:** This small randomized trial shows no significant difference in local survical and toxicity between 5FU-CDDP and CDDP alone conbined with RT in ACC. CDDP alone which has an excellent tolerance could be tested on a large scale for T1-2 NO tumors of the ACC.

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## Complete peritonectomy associated with intra peritoneal hyperthermic perfusion in the treatment of Pseudomyxoma Peritonei: Experience at the National Cancer Institute of Milan

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**Introduction:** Pseudomyxoma Peritonei is a rare disease characterized by a complete redistribution of mucin into the peritoneal cavity. Pseudomyxoma Peritonei could be classified into three diagnostic categories: disseminated peritoneal adenomucinosis (DPAM), peritoneal mucinous carcinomatosis (PMCA) and Intermediate Group (IG). DPAM is characterized by little cytologic atypia or mitotic activity often associated with an appendiceal mucinous adenoma, while PMCA shows cytologic features of adenocarcinoma. The intermediate group shows features between DPAM and PMCA and derived from well-differentiated appendiceal or intestinal mucinous adenocarcinoma.

Procedures: The natural history of PMP was strongly modified by the introduction of a new methodology proposed by Sugarbaker: the cytoreductive surgery that may require six peritonectomy procedures associated with Intra Peritoneal Hyperthermic Perfusion (IPHP) that combines hyperthermia and high drugs doses. Since November 1996, 12 patients with PMP syndrome have undergone surgical procedure in order to be treated by Sugarbaker's technique. Six cases were classified as DPAM, 4 as PMCA and finally 2 as intermediate histology. In the DPAM group three patients underwent appendicectomy before.

**Results:** All DPAM patients have been treated by Complete Peritonectomy and IPHP. Into the intermediate histology group 1 patient received Complete Peritonectomy and IPHP while 1 patient previously treated elsewhere 3 times by surgery received only induction IPHP. Unfortunately no patients in the PMCA group were eligible for the proposed treatment and received only an explorative laparotomy and partial debulking. IPHP was conducted by the closed abdomen technique using CDDP and MMC. All patients showed high CEA marker values that drastically decreased in those treated by Complete Peritonectomy and IPHP. All treated patients are NED.

**Conclusion:** Patients with PMP originated from undifferentiated mucinous adenocarcinoma were not eligible for this technique. Complete Peritonectomy associated with IPHP is the most indicated approach to cure this rare disease. This study was partially supported by the Associazione Italiana per la Ricerca sul Cancro.

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## Concurrent high dose radiotherapy and cisplatinum-based chemotherapy ± immunotherapy versus radiotherapy alone in esophageal carcinoma. Molecular biology in assesment of response to chemoradiotherapy

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**Purpose**: In current study, we compared concurrent chemoradiotherapy (CRT) ± Immunotherapy to radiotherapy alone (RT) in patients with esophageal Ca. Molecular biology including DNA ploidy status, SPF and

serum p53 in assessment of response to therapy and as prognostic factors were studied in the CRT group.

**Materials & Methods:** Two groups of esoph. Ca patients each compromized 40 patients were studiedú A prospective GI patients were randomly allocated to receive either Conc. CRT with CDDP, 5FU & MIT.C (20 patients GIA) or the same CRT + $\alpha$-INF (20 patients GIB). Responding patients at 40 Gy, received further RT of 25 Gy as a boost. Non-responders (NR) were submitted to transhiatal esophagectomy. We compared this prospective CRT GI to a retrospective GII of 40 patients treated with RT (65 GY).

**Results**: Patients characteristics were as follows: Squamous Ca 70% vs 75%, weight loss $\geq$10% of body weight 52.5% vs 60%, PS scale $\geq$ 70 was 60% vs 70% while scale 60 was 35% vs 30%, stage II 40% vs 25%, stage III 60% vs 75%, T2 15% vs 7.5%, T3 70% vs 65%, T4 15% vs 27.5%, N1 category was 62.5% vs 55% in GI and GII respectivelyú In group I (CRT) diploid tumors constituted 79.4% and aneuploid tumors 20.6%, high SPF tumors 26.4%, while low SPF 73.5%. The mean pretreatment serum value of p53 was 0.44 and 0.12 in a control group. The recorded overall response rate (CR + PR) was 72.5% in CRT:GI and 50% in RT:GII ($p < 0.05$ S). CR was achieved in 37.5% in GI (40% in GIA & 35% in GIB) vs 7.5% in GII. NR constituted 27.5% vs 50% in both CRT & RT groups. Diploid tumors responded much better than aneuploid tumors (77.8% vs 42.87%). There was rapid decline in the mean pre-treat. value of SPF at 40 Gy & at end of all treatment in responders. We found a statistically sign. rise in p53 antibodies in sera of NR. The 2-year OS was 37.5% for (CRT) GI vs 7.5% for RT alone ($p < 0.001$ HS). The 2-year progressive free survival (PFS) was 20% vs 2.5 in both groups ($p < 0.001$-HS), while mean survival was 14.5 $\pm$ 9.04 mo for CRT vs 7.07 $\pm$ 5.81 mo for RT. ($p < 0.001$ HS). There was no diff. regarding OS, PFS and mean duration of survival in subgroup GIA & GIB. The addition of $\alpha$-IFN improved response rate in patients with adeno Ca, those with diploid tumors (11/13) and those with low SPF (9/12). P.S., initial weight loss prior to therapy, stage of disease and response to therapy were the only statistically sign. factors which affectd the OS and PFS

**Conclusion**: Conc. CRT approach is superior to RT alone in treatment of non-met-esoph. Ca. The addition of $\alpha$-IFN improved results in adeno Ca, low SPF and those with diploid patternú Diploid tumors responded much better to CRT than aneuploid tumors. Rapid decline in mean pretreat. value of SPF is predictive of good response to CRT, while elevated serum levels of mutant p53 is indicative of poor response at 40 Gy.

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## Prognostic value of tumor suppressor gene (P53) and multiple drug resistance transport protein (P170) in hepatocellular carcinoma (HCC)

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**Purpose:** P53 and p170 was studied in HCC in an attempt to clarify their prognostic value and their role in the pathogenesis & resistance to therapy.

**Methods:** Liver biopsies from 47 unresectable HCC patients were examined for grades (G), HBV marker, staining for p53 and p170 using specific monoclonal antibodies. Treatment was systemic, intrahepatic and supportive only in 13, 19 and 15 patients respectively.

**Results:** Patients were 40 and 7 females with median age of 55 y. Tumor grades were GI in 10 (21%), GII in 22 (47%), GIII in 15 (32%) patients. Cirrhosis was found in 27 and AFP was elevated in 39 patients. HBsAg positive was found in 14 (30%) and Orcein stain was positive in 27 (57.4%) patients. Positive p53 was detected in the nuclei of 18 cases (38%) and 39 (83%) showed expression of p170. There was no significant correlation between p53 expression and age, sex, liver cirrhosis, positive HBsAg, AFP or response to chemotherapy. Positive p53 was directly related to tumor grade as 10% of GI, 22.7% of GII and 80% of G III showed positive p53. Patients with p53 positive had poor 1-year survival ($p = 0.01$) and p170 showed a strong parallel relation to short, survival ($p = 0.002$).

**Conclusion:** It was concluded that p53 and p170 expressions were directly related to short survival and poor prognosis in patients with HCC. P53 expression was related to the tumor grades and could be a late event in hepatocarcinogenesis.

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## 3D-conformal radiotherapy (3D-CRT) for pancreatic cancer: Acute toxicity and quality of life in the experience of the European Institute of Oncology

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**Purpose:** To evaluate tolerability and acute toxicity of 3D-CRT in pancreatic carcinoma.

Patients & Methods: Between December 1995 and February 1999, 25 patients with locally advanced pancreatic adenocarcinoma were treated with 3D-CRT. All patients were treated in a supine position with a 4-field technique (4 coplanar beams at 0°, 90°, 180°, 270°). For reproducible positioning, custom-made polyurethane foam casts were produced for each patient. The shaping of the beam apertures was realized by a multi-leaf collimator. The total target dose of the first part of the treatment was prescribed at the ICRU point and was 45 Gy for the pancreatic tumor delivered by a 15 MV linear accelerator in 25 fractions and days. A boost to the tumor with a margin of 1 cm around the target on BEV (16.2 Gy, 9 fractions) raised the total dose up to 61.2 Gy.

**Results:** The treatment was very well tolerated. No worsening of the initial performance status was observed, except for a patient who died after two weeks of treatment due to rapid progression of the disease in the liver. 7 patients who were complaining of severe abdominal pain at the beginning of radiotherapy got a remarkable improvement after the third week of radiation treatment and for 4 patients the pain disappeared completely. A transient diarrhoea was observed in 4 patients: the symptoms lasted no more than five days and resolved with medications. 5 patients suffered of transient nausea during the fourth-fifth week of treatment, but no vomit episodes were observed.

Weight loss of more than 10% of the initial weight was observed in 3 patients.

**Conclusion:** 3D-CRT on pancreas has an excellent acute toxicity profile even in patients with usually poor performance status.

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## A randomised trial of brachytherapy before (BRYB) and after (BRYA) external beam irradiation (XRT) for carcinomas of the oesophagus and cardia

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**Purpose:** To compare the results of BRYB and BRYA XRT in treatment of carcinoma of oesphagus and cardia.

**Methods:** From 1988–92 194 patients were prospectively randomised to BRYB or BRYA. Assessment included oesophagoscopy and biopsy, CT, barium studies and bronchoscopy, where indicated. Between groups, the distribution of patient/tumour characteristics were similar. The radiation dose was: XRT: 40 Gy/15#/3 weeks and brachytherapy: 15 Gy at 1 cm from the central axis, with no chemotherapy used.

**Results:** 50% of BRYB and 56% of the BRYA group received esophagectomy. Histology showed 15/59 (25%) of the BRYB and 20/61 (33%) of the BRYA group with no viable tumour ($p = 0.38$). Overall, 23/64 (36%) of squamous cancers and 12/56 (21%) of adenocarcinomas were considered sterilised. Actuarial cancer specific survival rates were identical (19% at 5 years), however for T3 tumours, there was a trend towards better survival in the BRYA patients (5 yr rate 14 v 9%, $p = 0.12$).

**Conclusions:** The resection rate, the sterilisation rate of preoperatively treated tumours and the survival rate for T3 tumours was slightly higher in BRBA patients, but these differences did not reach statistical significance.