control-group a decrease from 118 ml/min (66–174) to 88 ml/min (60–157) was observed ($p < 0.05$). The incidence of low Mg serum levels during treatment was 10% with AMI vs. 63% in control pts ($p < 0.05$). Mg levels recovered almost completely in both group at the end of cycles (94% vs. 83% of starting levels).

Conclusion: The use of early urinary markers allows to detect tubular kidney alterations even after the first application of P/IFO. AMI was identified to have protective effects against P/IFO associated nephrotoxicity indicating by significantly reduced urinary excretion of LMW/NAG, constant levels of Cc after 2 therapy cycles and a lower incidence of hypomagnesemia.

57 ORAL

Effectiveness of antiemetic drugs in prevention of chemotherapy (CT)-induced acute emesis

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Purpose: Efficacy obtained by treatment in clinical trials can be different from that achieved in daily practice. No data on this problem, at least for antiemetic treatment of CT-induced emesis, are available. A prospective drug utilization study at 33 Italian oncological centers.

Methods: In June 1996, for two consecutive weeks, all adult patients (pts) starting any CT, were blindly monitored for antiemetic prescription. Excluded from the study were pts with acute leukemia and pts receiving high dose CT or radiotherapy. Response to antiemetic therapy was evaluated by interviewing pts by phone 24 hrs after.

Results: 1220 patients (pts) receiving one-day CT were evaluable. Complete protection from vomiting/nausea was obtained in 75.7%/61.4% of 140 pts receiving cisplatin (CDDP)-based CT, in 81.8%/52.6% of 742 pts receiving moderately emetogenic CT (MEC) (carboplatin, epirubicin, doxorubicin, cyclophosphamide and mitoxantrone) and in 91.7%/71.6% of 338 pts receiving low emetogenic CT (i.e., gemcitabine, vincristine, vinblastine, vinorelbine, etc.). Complete protection from vomiting/nausea in pts receiving CDDP was 79.4%/68.2% if they received the standard combination of corticosteroids plus a 5-HT_3 receptor antagonist and 63.6%/39.4% if not, while in pts receiving MEC it was 84.7%/79.7% and 56.4%/49.8%, respectively.

Conclusion: The rate of protection from emesis achieved in these patients is not different from that obtained in those enrolled in clinical trials despite the fact that a great variety of doses and schedules of the various antiemetics (in particular corticosteroids) was observed.

58 ORAL

Lung cancer after therapy of Hodgkin disease: Influence of treatment and smoking

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Purpose: To retrospectively evaluate the risk of lung cancer after therapy of Hodgkin's disease in a single institution.

Methods: Medical records of 2,391 patients receiving therapy for Hodgkin's disease from 1961 to 1993 (mean follow-up, 10.6 years) were analyzed. Risks for lung cancer incidence were calculated by comparison with expected rates for the general population matched by age and race.

Results: From 1961 to 1993, 41 patients developed lung cancer, yielding a relative risk of 8.96 (95% confidence interval [CI] = 6.2–11 7). Relative risk was 7.2 (95% CI = 4.3–9.0) after radiotherapy alone, 10.7 (95% CI = 5.9–16) following chemoradiotherapy, and 11.0 (95% CI = 4–24.5) after salvage chemotherapy following radiotherapy. No one treated with chemotherapy alone developed lung cancer. Forty of 41 lung cancers (97.6%) arose in the irradiated field. Thirty-eight of the 41 patients (92.7%) had a history of smoking.

Conclusions: Lung cancers arose predominantly in the irradiated field and were strongly associated with smoking. Limiting the lung volume irradiated and avoiding smoking may reduce the subsequent risk of lung cancer.

59 POSTER

Protection of salivary glands by amifostine in patients treated with high dose radioiodine

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Purpose: Salivary gland impairment following high dose radioiodine treatment (HD-RIT) is a well recognized side effect. Since differentiated thyroid cancer (DTC) has a very good prognosis reduction of long-term side effect becomes more important. Therefore, the radioprotective effect of amifostine (Ethyol®) was investigated in patients receiving high dose radioiodine therapy.

Methods: Quantitative salivary gland scintigraphy was performed in 17 patients with DTC prior to and 3 months after radioiodine therapy with 6 GBq I-131. Eight patients were treated with 500 mg per sqm b.s. prior to radioiodine, and 9 patients served as control.

Results: In 9 controls HD-RIT significantly ($p < 0.01$) reduced pertechnetate uptake by 37% and 31% in parotid and submandibular glands, respectively. Three out of these 9 patients exhibited xerostomia grade I. In contrast, in 8 patients treated with amifostine there was no significant ($p = 0.878$) decrease in parenchymal function following HD-RIT, and xerostomia did not occur in any of them.

Conclusion: Parenchymal damage in salivary glands induced by HD-RIT can be reduced significantly by amifostine. This may help to increase quality of life of these patients.

60 POSTER

Effect of 5-fluorouracil (5-FU) infusion in myocardial perfusion scans

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Purpose: The cardiotoxicity of 5-FU is frequent (12.5%) and manifests usually by acute coronary events. The aim of this study was to assess the effect of the drug in the coronary blood flow.

Methods: During a 40 months period, 45 patients (M/F: 39/6, mean age: 59 years) with advanced head and neck cancer and normal cardiac function were included prospectively in a chemotherapeutic protocol with continuous IV infusion of 5-FU 1000 mg/m^2/day for 5 consecutive days. The evaluation of the myocardial perfusion was based on dipyridamole thallium-201 cardiac imaging and included 2 scans for every patient: (1) a dipyridamole thallium-201 heart scan before the initiation of chemotherapy, and (2) after one month, using the same imaging protocol and the same doses of dipyridamole and thallium-201, a heart scan while the patient was under the continuous IV infusion of 5-FU (3rd–4th day). The comparison of the 2 scans and the quantification of the results were based on the computer programme of the University of Alabama.

Results: There was a statistically significant decrease in the myocardial thallium-201 uptake during the IV 5-FU infusion ($p < 0.001$). This decrease was equivalent to 24.5% and was equal in all myocardial segments.

Conclusion: The infusion of high doses of 5-FU results in a great reduction (24.5%) of the myocardial perfusion. This effect could trigger the acute cardiotoxicity events observed mainly in patients with preexisting critical coronary stenoses.

61 POSTER

Intensive radiochemotherapy (RCT) with amifostine (A) in head and neck (H&N) cancer

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Purpose: We evaluated the ability of A to protect against the toxicities induced by intensive RCT for H&N cancer in a 3 arm study.

Methods: 25 patients with H&N cancer received primary or adjuvant radiotherapy (2Gy, 5days/week to 60Gy) and either carboplatin 70 mg/m^2 on days 1–5 and 21–25 (arm A, n = 10) or, carboplatin 70 mg/m^2 on days 1–5 and 21–25 and 5-FU 600 mg/m^2 administered over 16 hours on days 1–5 and 21–25 (arm B, n = 8). Both groups of patients received 500 mg A prior to carboplatin. Patients in arm C (n = 7) received chemotherapy as in arm B plus an additional dose of A (250 mG) prior to each infusion of 5FU.

Results: In a prior study where patients received RCT as in arm A but without A, 12/14 (86%) patient developed grade 3/4 mucositis and all patients developed grade 2 acute xerostomia (Buntzel, Blood 80 (10) suppl 1). In this study no patients in arms A, B or C developed grade 3/4 mucositis and only 1 patient in arm B developed grade 2 acute xerostomia. Haematological toxicity was minimal.

Conclusion: A, substantially reduces the toxicities associated with RCT for H&N cancer and allows the administration of intensive treatment. Additional experience is required to assess the benefits of a split dose of A.

62 POSTER

Functional Folate Status as a Prognostic Indicator of Toxicity in Clinical Trials of the Multitargeted Antifolate LY231514

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Studies in animal models and humans have revealed that folate nutritional status may be correlated with toxicity and antitumor activity of antifolates. Supplemental folic acid may play a role in protecting against the toxicities associated with antifolate drugs.

LY231514 is a multi-targeted antifolate that inhibits Thymidylate synthase, Dihydrofolate reductase and Glycinamide ribonucleotide formyltransferase. Functional folate status, based on serum concentrations of homocysteine (HCYS), cystathione (CYSTAT), and methylmalonic acid (MMA), was assessed in 118 patients participating in Phase 2 studies of LY231514. Samples were taken prior to initiation of therapy and prior to the start of each cycle. CTC toxicity scores (hematologic and non-hematologic) were assigned at the end of each cycle of therapy. Folate deficiency (elevated HCYS and CYSTAT and normal MMA) was observed in 11 patients. Eight of the folate deficient pts had CTC grade 3 or 4 toxicity and 3 of the folate deficient pts had only minor toxicity. Eight of the 11 pts experienced grade 4 neutropenia and 5 of the 11 pts experienced grade 4 thrombocytopenia. From this data, we would conclude that functional folate status may be a reliable prognostic indicator of hematologic toxicity in pts treated with LY231514. Further investigation is warranted to support this conclusion.

63 POSTER

Prevention of anti-androgen induced gynecomastia in prostate cancer: Clinical experience in 85 patients treated with 12GY single dose electron irradiation

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Purpose: The most common side effects of endocrine treatment in prostate cancer are breast tenderness and gynecomastia. Pre-irradiation prevents gynecomastia in males who receive feminizing hormones. Recommended doses range from 9 to 23, 75Gy in one to three fractions using x-rays or Co-60. Little is known about the efficiency and possible late sequela of single dose electron therapy and the role of pre-irradiation in androgen withdrawal.

Methods: From 1January to 31Dezember 1990 217pts. with prostate cancer received pre-irradiation of the breast in our Department. Median age: 75 yrs. Dose: 12Gy or 13Gy. Field size: 6 cm. All patients were treated with single dose 4 MeV or 6 MeV electrons. In autumn 1996 a questionnaire was mailed to the surviving patients to evaluate efficiency and long-term tolerance.

Results: 85pts. (39.2%) underwent evaluation, 79pts. (36.4%) had died and 53pts. (24.4%) were lost to follow-up. 11/85 showed a mild gynecomastia (12.9%). No mammalgia occurred. Erythema was reported by 13/85pts. (15.3%). In 8/85pts. mild pigmentation persisted (9.4%).

Conclusions: (1) Single dose electron treatment with 12Gy is as effective as fractionated schedules to prevent gynecomastia and mammalgia.

(2) Side effects are mild and well tolerated.

(3) The single dose treatment is easier accepted by elderly patients. A major problem of fractionated therapy, namely withdrawal of the patient during therapy, is avoided.

64 POSTER

Efficacy and safety of oral granisetron vs IV ondansetron in prevention of moderately emetogenic chemotherapy-induced nausea and vomiting

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Purpose: A multicenter, double-blind, parallel-group study compared the prophylactic efficacy and safety of 2-mg oral granisetron (G) vs 32-mg IV ondansetron (0) given once before cyclophosphamide- or carboplatin-based chemotherapy.

Methods: Chemo-naive pts (866 F. 219 MI) received two 1-mg G tablets (n = 542) or placebo at 60 min pre-chemo, and a 15-min infusion of 0 (n = 543) or placebo at 30 min pre-chemo. Dexamethasone or methylprednisolone were permitted. Primary endpoint was total control (no emesis, nausea, or use of antiemetic rescue medication) at 24 and 48 h after start of chemo. Secondary endpoints were incidence of emesis and nausea (+ incidence of antiemetic rescue) at 24 and 48 h. Safety was assessed up to 11 days post-chemo.

Results: Comparable efficacy was shown for all endpoints ($p < 0.0001$):

	24 Hours		48 Hours	
	Oral G	IV 0	Oral G	IV 0
Total Control (%)	59.4	58.0	46 7	43.8
No Emesis (%)	71.0	72 6	58.7	59.1
No Nausea (%)	60.0	58 4	47 4	44.4

Adverse experiences were similar in both groups, except for dizziness (5.4% G- vs 9.6% 0-treated pts; $p = 0.011$) and abnormal vision (0.6% G-vs 4.2% 0-treated pts; $p < 0.001$).

Conclusion: G tablets provided comparable efficacy to IV 0 in chemo-naive pts receiving moderately emetogenic chemotherapy. Both agents were well tolerated. (Supported by SmithKline Beecham)

65 POSTER

Cardiac function late after anthracycline (AX) therapy for pediatric cancer. A multicentric study of the german society of pediatric oncology and hematology (GPOH)

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Purpose: To define the incidence of cardiac abnormalities among previously asymptomatic patients late after AX therapy for pediatric cancer given according to GPOH protocols. To evaluate follow-up techniques in a multicentric setting.

Methods: Multicentric evaluation of relapse-free survivors who had no congenital heart-disease, no mediastinal irradiation, and did not receive cardiac medication by questionaire, physical exam, ECG, and echocardiogram (ECHO).

Results: 129 eligible patients who had been 9.5 ± 5.5 years of age at diagnosis of malignancy were evaluated 7.8 ± 3.2 after receiving a mean cumulative AX dose 250 ± 126 mg/m^2 (all < 500). While no patient had clinical signs suggestive of congestive heart failure, the fractional shortening rate FS measured by ECHO was subnormal (<28%) in 14 (10.9%). Higher than average cumulative AX dose ($p = 0.001$) and longer follow-up ($p < 0.05$), to a lesser extent higher individual AX dose ($p < 0.1$) and younger age at treatment ($p < 0.1$), but not patient sex, were associated with lower FS values. Various other echocardiographic or electrocardiographic measurements (incl. corrected QT-interval) did not show similarly strong correlations to known risk factors for AX cardiomyopathy.

Conclusion: Subclinical cardiac damage is frequent late after presumably safe cumulative AX doses, even when patients are asymptomatic. In a multicentric setting, more sophisticated measures of cardiac function were not superior to FS determination by ECHO.