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/m² (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.