$IR_{50}$and IR_{50A} groups received 50 Gy doses. The amifostine groups, C_A, $IR_{25A}$and IR_{50A}, were also incubated with 3 mg/mL amifostine for 15 minutes before irradiation. C group cells delivered neither radiation nor amifostine.
All groups were incubated in 37ºC and 5% CO_2 pressure for 12 hours. Prior to and 12 hours following the irradiation all samples were assessed in terms of total viable cell counts, colony numbers detected in mixed colony cultures and percentage of apoptosis by flow cytometry. The group means were compared for statistical analysis and significance level was set at $p < 0.05$.
Results: There was no statistical difference found for all assessments between control groups of C and C_A. Meanwhile, viable cell counts were detected higher in amifostine groups than those irradiated only ($0.9x10^9$/L, IR_{25} vs. 3.9 $x10^9$/L, IR_{25A}, $p<0.01$; 0.2 x 10^9/L, IR_{50} vs. 2.5×10^9/L, IR_{50A}, $p < 0.05$). In addition, the colony numbers were significantly higher in both dose levels (80, IR_{25A} vs. 20, IR_{25}, $p < 0.01$; 41, IR_{50A} vs. 12, IR_{50}, $p < 0.05$). The percentage of apoptosis was less in amifostine group but only for 25 Gy (46.0%, IR_{25A} vs. 29.7%, IR_{25}, $p < 0.05$).
Conclusions: Purging the malignant cells from stem cell grafts is done with several pharmacological agents and there are some data on amifostine preventing the normal bone marrow cells in procedure. Our study showed radiation may safely be administered in 25 Gy for the same purpose but with an amifostine like protector and further in vivo studies are required to test the feasibility.

Head and Neck Cancer

Oral presentations (Tue, 1 Nov, 13.45–15.45)
Head and neck cancer

994 ORAL

Paclitaxel and gemcitabine vs. paclitaxel and pegylated liposomal doxorubicin in advanced non–nasopharyngeal head and neck cancer. A phase III study conducted by the Hellenic Cooperative Oncology Group (HeCOG)

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Background: Advanced head and neck cancer (HNC) is an incurable disease and bears grave prognosis. Median survival with platinum-based chemotherapy does not exceed 6 months. In a series of phase II studies, we have shown that the combinations of paclitaxel (P) with gemcitabine (GEM) or with pegylated liposomal doxorubicin (PLD) have promising activity in patients with HNC. Median survival with these combinations, were 9 and 7.9 months respectively. The aim of the present study was to compare the efficacy of these two novel regimens with proven activity in phase II studies in patients with non-nasopharyngeal advanced HNC.
Patients and methods: From 15/9/1999 until 9/11/2004, 159 eligible patients entered the study. 5 patients presented with locally advanced and 154 with recurrent /metastatic disease. Patients randomized to Group A (n = 83) were treated with 6 cycles of P 175 mg/m^2 by 3-hour infusion on day 1 and GEM 1000 mg/m^2 on days 1, 8 of each cycle every 3 weeks. Patients randomized to Group B (n = 76) received 6 cycles of P, as in Group A, and PLD (Caelyx®) 40 mg/m^{2}every 4 weeks.
Results: There were 139 men and 20 women with a median age of 64 years and median PS of 1. Primary tumor site was larynx (48 vs. 46), hypopharynx (7 vs. 4), oropharynx (2 vs. 1), oral cavity (24 vs. 21), and other (2 vs. 4). 37 (45%) patients in Group A and 34 (45%) in Group B completed 6 cycles of chemotherapy. In 158 evaluable for response patients, the overall response rate was 20.5% vs. 29% (p = 0.215). After a median follow-up of 33.1 months, median time to progression was 4.4+ vs. 6.3+ months (p = 0.0568) and median overall survival (OS) 8.6 vs. 11.5+ months (p = 0.2784) in Group A and B, respectively.
Major (grade 3–4) toxicities included leukopenia (7.2% vs. 6.8%), anemia (0% vs. 3%), allergic reactions (1% vs. 7%, p = 0.02), peripheral neuropathy (1% vs. 0%), diarrhea (1% vs. 0%), infection (2% vs. 0%), fatigue (1% vs. 0%), skin (0% vs. 5.5%, p = 0.045), fever (2% vs. 1.4%), and hand and foot syndrome (0% vs. 3%). The incidence of neutropenia (12%), thrombocytopenia (1%) and pain (1%) was similar in the two groups. Alopecia was universal.
Conclusions: The present study has clearly demonstrated that there was no significant difference in OS between the two groups. Further, both regimens are accompanied with confirmed promising efficacy in advanced HNC and should be compared with the reference regimen of cisplatin and 5-day continuous infusion of fluorouracil.

995 ORAL

A phase II trial of BAY 43–9006 in patients with recurrent and/or metastatic head and neck squamous cell carcinoma (HNSCC). A Southwest Oncology Group (SWOG) trial

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Background: BAY 43–9006 is a potent raf kinase inhibitor of kinases of Raf-1 and B-Raf of the RAS/RAF/MEK/ERK pathway. The compound also inhibits protein tyrosine kinases associated with VEGFR-2 and 3 as well as PDGFR-B. We conducted a phase II trial to evaluate the efficacy of BAY 43–9006 in chemotherapy naive patients with metastatic or recurrent HNSCC.
Methods: Chemotherapy naïve patients with histologically proven squamous cell carcinoma of the head and neck either metastatic, persisted or recurred following definitive surgery and/or radiation therapy, and not amenable to salvage surgical resection with measurable disease were eligible. Patients must not have received any previous chemotherapy for the recurrent or metastatic disease. Patients who have received induction or adjuvant chemotherapy are eligible, provided that at least six months have elapsed since the last course of chemotherapy was administered. Patients may have received only one induction or adjuvant regimen. Patients must have adequate cardiac, hematologic, renal and hepatic function and a Zubrod Performance Status of 0 or 1. We obtained specimens from either archival or fresh pre-treatment biopsies and planned to obtain a second tissue specimen at the time of progression of disease for biologic correlative studies. BAY 43–9006 was administered orally at 400 mg BID on a continuous basis, in 28-day cycles. Respnses were evaluated every 8 weeks according to RESIST criteria.
Results: Twenty-two patients (17 males, 5 females, median age 65 years) have been enrolled to date. Fourteen patients are evaluable for toxicity. The drug was generally well tolerated. The grade 3 toxicities included one patient with hand/foot syndrome and another with stomatitis. The most common grade 2 toxicity was fatigue (3 pts.), and anorexia (3 pts.), nausea (1 pt), weight loss (1 pt), lymphopenia(1 pt), AST/ALT elevation(1 pt), and stomatitis (1 pt). The trial was temporarily closed on April 1, 2005 after reaching its first stage accrual goal and will reopen if any responses are documented.
Conclusion: BAY 43–9006 is well tolerated. Updated toxicity data will be reported. Response, time to progression and survival data will be presented, if the trial has met its final accrual goal and has permanently closed. If any response is noted the trial will re-open to accrue an additional 20 patients.

996 ORAL

Randomized phase III study in squamous cell carcinoma of the head & neck (SCCHN) using Lipoplatin: First safety results of a multicenter trial

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Background: Based on a metanalysis of >10.000 patients, cisplatin emerges as an essential chemotherapy drug for the treatment of advanced SCCHN. However, its clinical use is impeded by its severe adverse reactions, especially renal toxicity, peripheral neuropathy, and ototoxicity. In a randomized, multicenter phase III trial, we replaced conventional cisplatin by a liposomal formulation of cisplatin (lipoplatin), and compared the safety profiles of patients in the two treatment arms.
Material and methods: Main inclusion criteria selected patients with histologically confirmed SCCHN (primary metastatic or patients with relapsed/progressive disease) between 18–75 years of age with sufficient renal function defined as creatinine clearance >50 ml/min. After stratification (criteria: primary metastatic disease, recurrent or progressive SCCHN, prior chemotherapy, no prior chemotherapy, prior cisplatin-based chemotherapy, prior non-cisplatin based chemotherapy and center), patients were randomized between the following arms: Arm A: 100 mg/m^2/d lipoplatin (d 1, 8, 15) plus 1000 mg/m^2/d 5-FU (d 1–5) q3w for 6 cycles; arm B: 100 mg/m^2/d cisplatin (d 1) plus 1000 mg/m^2/d 5-FU (day 1–5) q3w for 6 cycles. Main endpoints for this interims analysis were hemato-, neuro- and nephrotoxicity. We tested for non-inferiority.

Results: In the lipoplatin arm, a total of 16 patients are evaluable after at least 2 cycles, while 14 patients are evaluable in the cisplatin arm. Demographic data are as follows: Men n = 27 (age 45–74 y, mean 55.5 y), women n = 2 (ages 47 y and 64 y). Haematotoxicity was more frequent in the cisplatin arm with leucopenia grade I/II in 7 cases and grade III/IV in 2 cases, while only 2 patients developed leucopenia (grades I/II) in the lipoplatin arm. Anemia was shown in either therapy arms: cisplatin and lipoplatin grade I: 2 pts and 4 pts, resp; grade II: 6 pts and 3 pts, resp; grade III: 2 pts and 2 pts, resp. Furthermore, 2 patients in the lipoplatin arm experienced renal toxicity of grade I as measured by a reduction of the creatinine clearance, while 6 patients showed a decrease of grade 2. Renal toxicity increased to 10 patients in the cisplatin arm (grade I: 4 pts; grade II: 4 pts; grade III: 4 pts). One case of ototoxicity occurred in the lipoplatin arm (grade IV) in contrast to 5 cases in the cisplatin arm (of grade II each). During cisplatin chemotherapy, 4 patients presented with grade I neurotoxicity, whereas only 2 patients developed neurotoxicity of grades I and III, each, in the lipoplatin arm.
Conclusion: Lipoplatin seems to reduce both the haematological and non-hematological toxicity profiles of cisplatin to a clinically relevant extent when combined with 5-FU. Because patients with advanced SCCHN have an increased risk of renal toxicity due to poor hydration, the observed reduction of side effects will influence the chance to preserve the dose density of chemotherapy, and thereby, the efficacy of treatment.

997 ORAL

Results of Intensity Modulated Radiotherapy (IMRT) in laryngeal and hypopharyngeal cancer: A dose escalation study

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Background: A study designed to determine the toxicity of dose-escalated IMRT using an accelerated RT schedule with concomitant chemotherapy.
Methods: Patients with T2–4, N1–3, M0 squamous cell carcinoma of the larynx or hypopharynx were recruited. A single-phase inverse-planned simultaneous boost was delivered by IMRT. In the first cohort 63 Gy/28F(daily) were delivered to the primary tumour and involved nodes and 51.8 Gy/28F to the elective nodal areas with concomitant Cisplatin, 100 mg/m^2 w1&5.
In cohort2, the primary tumour and involved nodes were dose escalated to 67.2 Gy/28F. Acute (NCICTCv.2.0) and late toxicity (RTOG and modified LENTSOM) was collected.
Results: 30 patients were entered, 15 in each cohort. For cohort 1, median age was 57 y(35–75), 9 larynx/6 hypopharynx. Complete response(CR) rate was 87%, with 13% partial response(PR) rate. At median follow up(FU) of 19 months(range 12–33), local recurrence occurred in 6 patients(40%): 5 in the high dose volume and 1 in the elective neck. Overall survival(OS) was 73% with a laryngeal preservation rate in the surviving patients of 82%. For cohort 2, median age was 66 y(60–85), 6 larynx/9 hypopharynx, and median FU 6 m(1–11). CR rate was 87% and PR 13%. No grade 4 toxicity was observed.
Acute toxicity is summarized in table 1. The typical pattern of radiation dermatitis observed was one of widespread erythema with dry and/or moist desquamation over the neck creases, which by week 4 post-RT had mostly settled, with 80% in cohort 1 and 85% in 2 having no toxicity at week4 post-RT. In cohort 1, 93% patients had dysphagia grade $\leqslant$2 by week 8 post-RT and 73% in cohort 2. G$\leqslant$1 pain was experienced by 93% patients by week 8 post-RT in cohort 1 and 82% in cohort 2.

Table 1: Grade 3 NCI CTC v.2.0 acute toxicity

	Cohort 1	Cohort 2
Radiation dermatitis	20%	15%
Dysphagia	60%	87%
Pain	30%	40%
Mucositis	47%	33%
Xerostomia	0%	7%

No severe late toxicity was seen in 87% patients. In cohort 1, 1 patient had G3 hoarseness at 18 m and 1 had G3 dysphagia at 6m that resolved to G1 by 1 y. At 1 y, 90% had xerostomia G0–1(LENTSOM). Maximum EORTC late toxicities were G2 dysphagia in 1 patient and G2 xerostomia in another. In cohort 2, 1 patient had G3 laryngeal toxicity and 1 G3 dysphagia at 6 m and 90% had xerostomia G0–1(LENT SOM). Maximum EORTC late toxicities at 6m were G3 dysphagia in 1 patient and G2 laryngeal toxicity in 2 patients.
Conclusions: Initial results of dose escalation with chemo-IMRT suggest high CR, OS and laryngeal preservation rates. Acute toxicity shows recovery over time and initial late toxicity is rare. Longer follow up is required to determine the incidence of late side effects.

998 ORAL

Longitudinal changes in quality of life and costs in long-term survivors of tumors of the oropharynx treated with brachytherapy or surgery

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Purpose: To assess the longitudinal changes in quality of life (QOL) and treatment costs in long-term survivors of oropharyngeal cancers treated with brachytherapy (BT) or surgery (S).
Materials and Methods: From 1991–2001, 144 patients with tonsillar fossa (TF) and/or soft palate (SP), and base of tongue (BOT) tumors, were treated by organ function preservation therapy, using external beam radiotherapy (EBRT) and BT. 110 patients not suitable for BT were treated by a combined resection with postoperative EBRT. Among all patients $\geqslant$2 and <10 years alive NED, a QOL survey was conducted in 2003 and repeated in 2005. Two groups were studied: group I TF/SP/BOT tumors treated by S (44), and group II TF/SP/BOT tumors treated by BT (75). The performance status scales scores for eating in public (EP), understandability of speech (SP), and normalcy of diet (ND) were determined. In addition, xerostomia ("dry mouth") and the (in)ability to swallow ("drink to eat"), were measured by standardized queries and a visual analogue scale. By regression analysis, the effect of time from diagnosis, age, dose, sex, T/N-stage, trismus, necrosis and treatment modality on the PSS scores was determined. 22 Patients of group I, and 27 of group II were eligible for analysis. In conjunction with the 2005 survey, the EORTC QLQ-C30, EORTC H&N35, and Euroqol (EQ5D) questionnaires were mailed. For each treatment group treatment costs were computed.
Results: In the 2003 survey EP, SP, and ND showed significant difference in BT as opposed to S. Over time, a significant difference was found for drink to eat and for ND for BT as opposed to S. For the QLQ-H&N35: S patients experience significantly more speech, teeth and opening mouth problems. Parameters significantly effecting the mean QoL scores were age, total dose, sex, trismus and treatment modality.
Mean costs: group I: €26,590, and group II: €16,112.
Discussion: The QOL surveys of this paper show that item for item the median scores did not significantly change in time. For each group, discriminating factors seem to be modality related and site specific (e.g. BT more ulceration, surgery more trismus, and for both modalities the dry mouth syndrome). Due to the number of admission days, S is more expensive as opposed to BT. Given the good tumor control for both treatment groups (BT and S); 85% at 10 years, the data suggest that QOL and associated costs, can be of additional value when discriminating between treatment modalities.

999 ORAL

The Chernobyl legacy: relationship between radiation exposure, RET rearrangement and BRAF mutation in childhood thyroid cancer

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There was a large increase in the incidence of papillary thyroid cancer inj those areas of Ukraine exposed to radioactive fallout following the Chernobyl Nuclear Power Plant accident in April 1986. This increase was most pronounced in those who were children at the time of the accident. Thyroid cancer is usually very rare in children (aged under 16 at operation). 131-I has a relatively short physical half-life (7 days) and the rate of thyroid cancer has dropped back to background levels (of the order of 1 per million per year) in those who were born after 1st January 1987. The Chernobyl Tissue Bank (www.chernobyltissuebank.com) was established in 1998 to collect biological samples from those aged under 19 (i.e.born after 26th April 1967) at the time of the accident who subsequently developed thyroid tumours and were resident in the areas of Ukraine and Russia most highly contaminated by radioiodine in fallout. The continued collection of material has allowed us to collect samples from children from the same geographical area, but born more than 9 months after the accident, and whose thyroid cancer therefore is not the result of exposure to radioiodine. This is a unique